Drive, Boulder, co 80301 (US). STINCHCOMB, Dan; 7203 Old Post Road, Boulder, CO 80301 (US). ESCOBEDO, Jaime; 1470 Livoma Road, Alamo, CA 94507 (US). (74) Agents: HELLENKAMP, Amy, S. et al.; Lyon & Lyon L.L.P., Suite 4700, 633 West Fifth Street, Los Angeles, CA 90071-

WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)							
(51) International Patent Classification ⁶ : C12N 15/11, 9/00, 5/10		A2	(11) International Publication Number: WO 97/15662				
			(43) International Publication Date: 1 May 1997 (01.05.97)				
(21) International Appli		S96/174	BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,				
(30) Priority Data:	23 October 1990	(23.10.9	Published				
60/005,974 08/584,040	26 October 1995 (26.10.95 11 January 1996 (11.01.96)	•	S Without international search report and to be republished upon receipt of that report.				
[US/US]; 2950 V	OZYME PHARMACEUTICAI Vilderness Place, Boulder, CO 80 ORATION [US/US]; 4560 Hort 94608 (US).	301 (US).				
	, Pamela; 705 Barberry Circle, . McSWIGGEN, James; 4866						

(54) Title: METHOD AND REAGENT FOR THE TREATMENT OF DISEASES OR CONDITIONS RELATED TO LEVELS OF VASCULAR ENDOTHELIAL GROWTH FACTOR RECEPTOR

(57) Abstract

2066 (US).

Nucleic acid molecule which modulates the synthesis, expression and/or stability of an mRNA encoding one or more receptors of vascular endothelial growth factor.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
ΑU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	IE	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE	Kenya	RO	Romania
BY	Belarus	KG	Kyrgystan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic	SD	Sudan
CF	Central African Republic		of Korea	SE	Sweden
CG	Congo	KR	Republic of Korea	SG	Singapore
СН	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LR	Liberia	SZ	Swaziland
CS	Czechoslovakia	LT	Lithuania	TD	Chad
CZ	Czech Republic	LU	Luxembourg	TG	Togo
DE	Germany	LV	Latvia	TJ	Tajikistan
DK	Denmark	MC	Monaco	TT	Trinidad and Tobago
EE	Estonia	MD	Republic of Moldova	UA	Ukraine
ES	Spain	MG	Madagascar	UG	Uganda
FI	Finland	ML	Mali	US	United States of America
FR	France	MN	Mongolia	UZ	Uzbekistan
GA	Gabon	MR	Mauritania	VN	Viet Nam

PCT/US96/17480 WO 97/15662

1

DESCRIPTION

Method and Reagent for the Treatment of Diseases or Conditions Related to Levels of Vascular Endothelial Growth Factor Receptor

Background Of The Invention

This application is a continuation-in-part of Pavco et al., U.S. Serial No. 60/005,974 all of which is hereby incorporated by reference herein (including drawings).

This invention relates to methods and reagents for the treatment of diseases or conditions relating to the levels of expression of vascular endothelial growth factor (VEGF) receptor(s).

The following is a discussion of relevant art, none of which is admitted to be prior art to the present invention.

VEGF, also referred to as vascular permeability factor (VPF) and vasculotropin, is a potent and highly specific mitogen of vascular endothelial cells (for a review see Ferrara, 1993 Trends Cardiovas. Med. 3, 244; Neufeld et al., 1994 Prog. Growth Factor Res. 5, VEGF induced neovascularization is implicated in various pathological conditions such as tumor angiogenesis, proliferative diabetic retinopathy, hypoxia-induced 20 angiogenesis, rheumatoid arthritis, psoriasis, wound healing and others.

VEGF, an endothelial cell-specific mitogen, is a 34-45 kDa glycoprotein with a wide range of activities that include promotion of angiogenesis, enhancement of 25 vascular-permeability and others. VEGF belongs to the platelet-derived growth factor (PDGF) family of growth factors with approximately 18% homology with the A and B chain of PDGF at the amino acid level. Additionally, VEGF contains the eight conserved cysteine residues common to all growth factors belonging to the PDGF family (Neufeld et al., supra). VEGF protein is believed to exist

30

predominantly as disulfide-linked homodimers; monomers of VEGF have been shown to be inactive (Plouet et al., 1989 $EMBO\ J.\ 8$, 3801).

VEGF exerts its influence on vascular endothelial cells by binding to specific high-affinity cell surface receptors. Covalent cross-linking experiments 125 I-labeled VEGF protein have led to the identification of three high molecular weight complexes of 225, 195 and 175 kDa presumed to be VEGF and VEGF receptor complexes (Vaisman et al., 1990 J. Biol. Chem. 265, 19461). Based 10 on these studies VEGF-specific receptors of 180, 150 and 130 kDa molecular mass were predicted. In endothelial cells, receptors of 150 and the 130 kDa have been identi-The VEGF receptors belong to the superfamily of fied. 15 receptor tyrosine kinases (RTKs) characterized by a conserved cytoplasmic catalytic kinase domain and a hydrophylic kinase sequence. The extracellular domains of the VEGF receptors consist of seven immunoglobulin-like domains that are thought to be involved in VEGF binding 20 functions.

The two most abundant and high-affinity receptors of VEGF are flt-1 (fms-like tyrosine kinase) cloned by Shibuya et al., 1990 Oncogene 5, 519 and KDR (kinase-insert-domain-containing receptor) cloned by Terman et al., 1991 Oncogene 6, 1677. The murine homolog of KDR, cloned by Mathews et al., 1991, Proc. Natl. Acad. Sci., USA, 88, 9026, shares 85% amino acid homology with KDR and is termed as flk-1 (fetal liver kinase-1). Recently it has been shown that the high-affinity binding of VEGF to its receptors is modulated by cell surface-associated heparin and heparin-like molecules (Gitay-Goren et al., 1992 J. Biol. Chem. 267, 6093).

VEGF expression has been associated with several pathological states such as tumor angiogenesis, several forms of blindness, rheumatoid arthritis, psoriasis and others. Following is a brief summary of evidence supporting the involvement of VEGF in various diseases:

25

25

- 1) Tumor angiogenesis: Increased levels of VEGF gene expression have been reported in vascularized and edemaassociated brain tumors (Berkman et al., 1993 J. Clini. Invest. 91, 153). A more direct demostration of the role 5 of VEGF in tumor angiogenesis was demonstrated by Jim Kim et al., 1993 Nature 362,841 wherein, monoclonal antibodies against VEGF were successfully used to inhibit the growth of rhabdomyosarcoma, glioblastoma multiforme cells in nude Similarly, expression of a dominant negative mutated form of the flt-1 VEGF receptor inhibits vascularization induced by human glioblastoma cells in nude mice (Millauer et al., 1994, Nature 367, 576).
- 2) Ocular diseses: Aiello et al., 1994 New Engl. J. Med. 331, 1480, showed that the ocular fluid, of a majority of patients suffering from diabetic retinopathy and other retinal disorders, contains a high concentration of Miller et al., 1994 Am. J. Pathol. 145, 574, reported elevated levels of VEGF mRNA in patients suffering from retinal ischemia. These observations support a direct role for VEGF in ocular diseases. 20
 - 3) Psoriasis: Detmar et al., 1994 J. Exp. Med. 180, 1141 reported that VEGF and its receptors were overexpressed in psoriatic skin and psoriatic dermal microvessels, suggesting that VEGF plays a significant role in psoriasis.
- 4) Rheumatoid arthritis: Immunohistochemistry and in situ hybridization studies on tissues from the joints of patients suffering from rheumatoid arthritis show an increased level of VEGF and its receptors (Fava et al., 1994 J. Exp. Med. 180, 341). Additionally, Koch et al., 30 1994 J. Immunol. 152, 4149, found that VEGF-specific antibodies were able to significantly reduce the mitogenic activity of synovial tissues from patients suffering from rheumatoid arthritis. These observations support a direct role for VEGF in rheumatoid arthritis.

In addition to the above data on pathological conditions involving excessive angiogenesis, a number of

4

studies have demonstrated that VEGF is both necessary and sufficient for neovascularization. Takashita et al., 1995 J. Clin. Invest. 93, 662, demonstrated that a single injection of VEGF augmented collateral vessel development in a rabbit model of ischemia. VEGF also can induce neovascularization when injected into the cornea. Expression of the VEGF gene in CHO cells is sufficient to confer tumorigenic potential to the cells. Kim et al., supra and Millauer et al., supra used monoclonal antibodies against VEGF or a dominant negative form of flk-1 receptor to inhibit tumor-induced neovascularization.

During development, VEGF and its receptors are associated with regions of new vascular growth (Millauer et al., 1993 Cell 72, 835; Shalaby et al., 1993 J. Clin. 15 Invest. 91, 2235). Furthermore, transgenic mice lacking either of the VEGF receptors are defective in blood vessel infact these mouse do not survive; flk-1 formation, appears to be required for differentiation of endothelial cells, while flt-1 appears to be required at later stages 20 of vessel formation (Shalaby et al., 1995 Nature 376, 62; Fung et al., 1995 Nature 376, 66). Thus, these receptors must be present to properly signal endothelial cells or their precursors to respond to vascularization-promoting stimuli.

All of the conditions listed above, involve extensive vascularization. This hyper-stimulation of endothelial cells may be alleviated by VEGF antagonists. Thus most of the therapeutic efforts for the above conditions have concentrated on finding inhibitors of the VEGF protein.

Kim et al., 1993 Nature 362, 841 have been successful in inhibiting VEGF-induced tumor growth and angiogenesis in nude mice by treating the mice with VEGF-specific monoclonal antibody.

Koch et al., 1994 J. Immunol. 152, 4149 showed that the mitogenic activity of microvascular endothelial cells found in rheumatoid arthritis (RA) synovial tissue explants and the chemotactic property of endothelial cells

from RA synovial fluid can be neutralized significantly by treatment with VEGF-specific antibodies.

Ullrich et al., International PCT Publication No. WO 94/11499 and Millauer et al., 1994 Nature 367, 576 used a soluble form of flk-1 receptor (dominant-negative mutant) to prevent VEGF-mediated tumor angiogenesis in immunodeficient mice.

Kendall and Thomas, International PCT Publication No. WO 94/21679 describe the use of naturally occuring or recombinantly-engineered soluble forms of VEGF receptors to inhibit VEGF activity.

Robinson, International PCT Publication No. WO 95/04142 describes the use of antisense oligonucleotides targeted against VEGF RNA to inhibit VEGF expression.

Jellinek et al., 1994 Biochemistry 33, 10450 describe the use of VEGF-specific high-affinity RNA aptamers to inhibit the binding of VEGF to its receptors.

Rockwell and Goldstein, International PCT Publication No. WO 95/21868, describe the use of anti-VEGF receptor monoclonal antibodies to neutralize the the effect of VEGF on endothelial cells.

Summary Of The Invention

The invention features novel nucleic acid-based techniques [e.g., enzymatic nucleic acid molecules (ribozymes), antisense nucleic acids, 2-5A antisense chimeras, triplex DNA, antisense nucleic acids containing RNA cleaving chemical groups (Cook et al., U.S. Patent 5,359,051)] and methods for their use to down regulate or inhibit the expression of receptors of VEGF (VEGF-R).

In a preferred embodiment, the invention features use of one or more of the nucleic acid-based techniques to inhibit the expression of flt-1 and/or flk-1/KDR receptors.

By "inhibit" it is meant that the activity of VEGF-R or level of mRNAs or equivalent RNAs encoding VEGF-R is reduced below that observed in the absence of the nucleic acid. In one embodiment, inhibition with ribozymes

6

preferably is below that level observed in the presence of an enzymatically inactive RNA molecule that is able to bind to the same site on the mRNA, but is unable to cleave that RNA. In another embodiment, inhibition with antisense oligonucleotides is preferably below that level observed in the presence of for example, an oligonucleotide with scrambled sequence or with mismatches.

By "enzymatic nucleic acid molecule" it is meant an RNA molecule which has complementarity in a substrate binding region to a specified gene target, and also has an enzymatic activity which is active to specifically cleave target RNA. That is, the enzymatic RNA molecule is able to intermolecularly cleave RNA and thereby inactivate a target RNA molecule. This complementary regions allow sufficient hybridization of the enzymatic RNA molecule to the target RNA and thus permit cleavage. One hundred percent complementarity is preferred, but complementarity as low as 50-75% may also be useful in this invention. By "equivalent" RNA to VEGF-R is meant to include those naturally occurring RNA molecules in various animals, including human, mice, rats, rabbits, primates and pigs.

By "antisense nucleic acid" it is meant a non-enzymatic nucleic acid molecule that binds to target RNA by means of RNA-RNA or RNA-DNA or RNA-PNA (protein nucleic acid; Egholm et al., 1993 Nature 365, 566) interactions and alters the activity of the target RNA (for a review see Stein and Cheng, 1993 Science 261, 1004).

By "2-5A antisense chimera" it is meant, an antisense oligonucleotide containing a 5' phosphorylated 2'-5'-linked adenylate residues. These chimeras bind to target RNA in a sequence-specific manner and activate a cellular 2-5A-dependent ribonuclease which, in turn, cleaves the target RNA (Torrence et al., 1993 Proc. Natl. Acad. Sci. USA 90, 1300).

35 By "triplex DNA" it is meant an oligonucleotide that can bind to a double-stranded DNA in a sequence-specific manner to form a triple-strand helix. Formation of such

25

7

triple helix structure has been shown to inhibit transcription of the targeted gene (Duval-Valentin et al., 1992 Proc. Natl. Acad. Sci. USA 89, 504).

By "gene" it is meant a nucleic acid that encodes an 5 RNA.

By "complementarity" it is meant a nucleic acid that can form hydrogen bond(s) with other RNA sequence by either traditional Watson-Crick or other non-traditional types (for example, Hoogsteen type) of base-paired interactions.

Six basic varieties of naturally-occurring enzymatic RNAs are known presently. Each can catalyze the hydrolysis of RNA phosphodiester bonds in trans (and thus can cleave other RNA molecules) under physiological condi-15 tions. Table I summarizes some of the characteristics of these ribozymes. In general, enzymatic nucleic acids act by first binding to a target RNA. Such binding occurs through the target binding portion of a enzymatic nucleic acid which is held in close proximity to an enzymatic portion of the molecule that acts to cleave the target 20 Thus, the enzymatic nucleic acid first recognizes and then binds a target RNA through complementary basepairing, and once bound to the correct site, enzymatically to cut the target RNA. Strategic cleavage of such a target RNA will destroy its ability to direct synthesis of an encoded protein. After an enzymatic nucleic acid has bound and cleaved its RNA target, it is released from that RNA to search for another target and can repeatedly bind and cleave new targets. Thus, a single ribozyme molecule is able to cleave many molecules 30 In addition, the ribozyme is a highly of target RNA. specific inhibitor of gene expression, with the specificity of inhibition depending not only on the base-pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches, or 35 base-substitutions, near the site of cleavage can completely eliminate catalytic activity of a ribozyme.

8

Ribozymes that cleave the specified sites in VEGF-R mRNAs represent a novel therapeutic approach to treat tumor angiogenesis, ocular diseases, rhuematoid arthritis, psoriasis and others. Applicant indicates that ribozymes are able to inhibit the activity of VEGF-R (specifically flt-1 and flk-1/KDR) and that the catalytic activity of the ribozymes is required for their inhibitory effect. Those of ordinary skill in the art will find that it is clear from the examples described that other ribozymes that cleave VEGF-R mRNAs may be readily designed and are within the invention.

In preferred embodiments of this invention, enzymatic nucleic acid molecule is formed in a hammerhead or hairpin motif, but may also be formed in the motif of 15 a hepatitis delta virus, group I intron or RNaseP RNA (in association with an RNA guide sequence) or Neurospora VS Examples of such hammerhead motifs are described by Rossi et al., 1992, AIDS Research and Human Retroviruses 8, 183, of hairpin motifs by Hampel et al., EP0360257, Hampel and Tritz, 1989 Biochemistry 28, 4929, and Hampel 20 et al., 1990 Nucleic Acids Res. 18, 299, and an example of the hepatitis delta virus motif is described by Perrotta and Been, 1992 Biochemistry 31, 16; of the RNaseP motif by Guerrier-Takada et al., 1983 Cell 35, 849, Neurospora VS 25 RNA ribozyme motif is described by Collins (Saville and Collins, 1990 Cell 61, 685-696; Saville and Collins, 1991 Proc. Natl. Acad. Sci. USA 88, 8826-8830; Collins and Olive, 1993 Biochemistry 32, 2795-2799) and of the Group I intron by Cech et al., U.S. Patent 4,987,071. 30 specific motifs are not limiting in the invention and those skilled in the art will recognize that all that is important in an enzymatic nucleic acid molecule of this invention is that it has a specific substrate binding site which is complementary to one or more of the target gene RNA regions, and that it have nucleotide sequences within or surrounding that substrate binding site which impart an RNA cleaving activity to the molecule.

In a preferred embodiment the invention provides a method for producing a class of enzymatic cleaving agents which exhibit a high degree of specificity for the RNA of a desired target. The enzymatic nucleic acid molecule is 5 preferably targeted to a highly conserved sequence region of target mRNAs encoding VEGF-R proteins (specifically flt-1 and flk-1/KDR) such that specific treatment of a disease or condition can be provided with either one or several enzymatic nucleic acids. Such enzymatic nucleic acid molecules can be delivered exogenously to specific tissue or cellular targets as required. Alternatively, the ribozymes can be expressed from DNA and/or RNA vectors that are delivered to specific cells.

Synthesis of nucleic acids greater than 100 nucleotides in length is difficult using automated methods, and 15 the therapeutic cost of such molecules is prohibitive. In this invention, small nucleic acid motifs (e.g., antisense oligonucleotides, hammerhead or the hairpin ribozymes) are used for exogenous delivery. The simple structure of these molecules increases the ability of the nucleic acid 20 to invade targeted regions of the mRNA structure. However, these nucleic acid molecules can expressed within cells from eukaryotic promoters (e.g., Izant and Weintraub, 1985 Science 229, 345; McGarry and Lindquist, 1986 Proc. Natl. Acad. Sci. USA 83, Sullenger-Scanlon et al., 1991, Proc. Natl. Acad. Sci. USA, 88, 10591-5; Kashani-Sabet et al., 1992 Antisense Res. Dev., 2, 3-15; Dropulic et al., 1992 J. Virol, 66, 1432-41; Weerasinghe et al., 1991 J. Virol, 65, 5531-4; Ojwang et al., 1992 Proc. Natl. Acad. Sci. USA 89, 30 10802-6; Chen et al., 1992 Nucleic Acids Res., 20, 4581-9; Sarver et al., 1990 Science 247, 1222-1225; Thompson et al., 1995 Nucleic Acids Res. 23, 2259). Those skilled in the art realize that any nucleic acid can be expressed in eukaryotic cells from the appropriate DNA/RNA vector. 35 activity of such nucleic acids can be augmented by their release from the primary transcript by a ribozyme (Draper

10

et al., PCT W093/23569, and Sullivan et al., PCT W094/02595, both hereby incorporated in their totality by reference herein; Ohkawa et al., 1992 Nucleic Acids Symp. Ser., 27, 15-6; Taira et al., 1991, Nucleic Acids Res., 19, 5125-30; Ventura et al., 1993 Nucleic Acids Res., 21, 3249-55; Chowrira et al., 1994 J. Biol. Chem. 269, 25856).

Such nucleic acids are useful for the prevention of the diseases and conditions discussed above, and any other diseases or conditions that are related to the levels of VEGF-R (specifically flt-1 and flk-1/KDR) in a cell or tissue.

By "related" is meant that the reduction of VEGF-R (specifically flt-1 and flk-1/KDR) RNA levels and thus reduction in the level of the respective protein will relieve, to some extent, the symptoms of the disease or condition.

Ribozymes are added directly, or can be complexed with cationic lipids, packaged within liposomes, or otherwise delivered to target cells or tissues. The nucleic acid or nucleic acid complexes can be locally administered to relevant tissues ex vivo, or in vivo through injection, infusion pump or stent, with or without their incorporation in biopolymers. In preferred embodiments, the ribozymes have binding arms which are complementary to the sequences in Tables II to IX. Examples of such ribozymes also are shown in Tables II to IX. Examples of such ribozymes consist essentially of sequences defined in these By "consists essentially of" is meant that the active ribozyme contains an enzymatic center equivalent to those in the examples, and binding arms able to bind mRNA such that cleavage at the target site occurs. sequences may be present which do not interfere with such cleavage.

In another aspect of the invention, ribozymes that cleave target RNA molecules and inhibit VEGF-R (specifically flt-1 and flk-1/KDR) activity are expressed from transcription units inserted into DNA or RNA vectors. The

20

25

recombinant vectors are preferably DNA plasmids or viral vectors. Ribozyme expressing viral vectors could be constructed based on, but not limited to, adeno-associated virus, retrovirus, adenovirus, or alphavirus. Preferably, 5 the recombinant vectors capable of expressing the ribozymes are delivered as described above, and persist in target cells. Alternatively, viral vectors may be used that provide for transient expression of ribozymes. vectors might be repeatedly administered as necessary. 10 Once expressed, the ribozymes cleave the target mRNA. Delivery of ribozyme expressing vectors could be systemic, such as by intravenous or intramuscular administration, by administration to target cells ex-planted from the patient followed by reintroduction into the patient, or by any other means that would allow for introduction into the desired target cell.

By "vectors" is meant any nucleic acid- and/or viral-based technique used to deliver a desired nucleic acid.

Other features and advantages of the invention will 20 be apparent from the following description of the preferred embodiments thereof, and from the claims.

Description Of The Preferred Embodiments

First the drawings will be described briefly.

Drawings

Figure 1 is a diagrammatic representation of the hammerhead ribozyme domain known in the art. Stem II can be ≥ 2 base-pair long.

Figure 2a is a diagrammatic representation of the hammerhead ribozyme domain known in the art; Figure 2b is a diagrammatic representation of the hammerhead ribozyme as divided by Uhlenbeck (1987, Nature, 327, 596-600) into a substrate and enzyme portion; Figure 2c is a similar diagram showing the hammerhead divided by Haseloff and Gerlach (1988, Nature, 334, 585-591) into two portions; and Figure 2d is a similar diagram showing the hammerhead

12

divided by Jeffries and Symons (1989, Nucl. Acids. Res., 17, 1371-1371) into two portions.

Figure 3 is a diagramatic representation of the general structure of a hairpin ribozyme. Helix 2 (H2) is 5 provided with a least 4 base pairs (i.e., n is 1, 2, 3 or 4) and helix 5 can be optionally provided of length 2 or more bases (preferably 3 - 20 bases, i.e., m is from 1 -20 or more). Helix 2 and helix 5 may be covalently linked by one or more bases (i.e., r is \geq 1 base). Helix 1, 4 or 5 may also be extended by 2 or more base pairs (e.g., 4 -20 base pairs) to stabilize the ribozyme structure, and preferably is a protein binding site. In each instance, each N and N' independently is any normal or modified base and each dash represents a potential base-pairing interaction. These nucleotides may be modified at the sugar, 15 base or phosphate. Complete base-pairing is not required in the helices, but is preferred. Helix 1 and 4 can be of any size (i.e., o and p is each independently from 0 to any number, e.g., 20) as long as some base-pairing is maintained. Essential bases are shown as specific bases 20 in the structure, but those in the art will recognize that one or more may be modified chemically (abasic, base, sugar and/or phosphate modifications) or replaced with another base without significant effect. Helix 4 can be 25 formed from two separate molecules, i.e., without a connecting loop. The connecting loop when present may be a ribonucleotide with or without modifications to its base, sugar or phosphate. "q" is ≥ 2 bases. The connecting loop can also be replaced with a non-nucleotide linker molecule. H refers to bases A, U, or C. Y refers to pyrimidine bases. " " refers to a covalent bond.

Figure 4 is a representation of the general structure of the hepatitis delta virus ribozyme domain known in the art.

Figure 5 is a representation of the general structure of the VS RNA ribozyme domain.

13

Figure 6 is a schematic representation of an RNAseH accessibility assay. Specifically, the left side of Figure 6 is a diagram of complementary DNA oligonucleotides bound to accessible sites on the target RNA.

5 Complementary DNA oligonucleotides are represented by broad lines labeled A, B, and C. Target RNA is represented by the thin, twisted line. The right side of Figure 6 is a schematic of a gel separation of uncut target RNA from a cleaved target RNA. Detection of target RNA is by autoradiography of body-labeled, T7 transcript. The bands common to each lane represent uncleaved target RNA; the bands unique to each lane represent the cleaved products.

Figure 7 shows the effect of hammerhead ribozymes targeted against flt-1 receptor on the binding of VEGF to 15 the surface of human microvascular endothelial cells. Sequences of the ribozymes used are shown in Table II; the length of stem II region is 3 bp. The hammerhead ribozymes were chemically modified such that the ribozyme 20 consists of ribose residues at five positions (see Figure 11); U4 and U7 positions contain $2'-NH_2$ modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions; four nucleotides at the 5' terminus contains phosphorothioate substitutions. Additionally, the 3' end of the ribozyme contains a 3'-3' linked inverted abasic 25 deoxyribose. The results of two separate experiments are shown as separate bars for each set. Each bar represents the average of triplicate samples. The standard deviation is shown with error bars. For the flt-1 data, 500 nM ribozyme (3:1 charge ratio with LipofectAMINE®) was used. 30 Control 1-10 is the control for ribozymes control 11-20 is the control for ribozymes 3008-5585. The Control 1-10 and Control 11-20 represent the treatment of cells with LipofectAMINE® alone without any ribozymes.

Figure 8 shows the effect of hammerhead ribozymes targeted against KDR receptor on the binding of VEGF to KDR on the surface of human microvascular endothelial

cells. Sequences of the ribozymes used are shown in Table IV; the length of stem II region is 3 bp. The hammerhead ribozymes were chemically modified such that the ribozyme consists of ribose residues at five positions (see Figure 11); U4 and U7 positions contain $2'-NH_2$ modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions; four nucleotides at the 5' terminus contains phosphorothicate substitutions. Additionally, the 3' end of the ribozyme contains a 3'-3' linked inverted abasic deoxyribose. The Control 1-10 and Control 11-20 represent the treatment of cells with LipofectAMINE® alone without any ribozymes. Irrel. RZ, is a control experiment wherein the cells are treated with a non-KDR-targeted ribozyme complexed with Lipofectamine®. 200 nM ribozyme (3:1 charge ratio with LipofectAMINE®) was used. In addition to the KDR-targeted ribozymes, the effect on VEGF binding of a ribozyme targeted to an irrelevant mRNA (irrel. RZ) is also shown. Because the affinity of KDR for VEGF is about 10-fold lower than the affinity of flt-1 for VEGF, a higher concentration of VEGF was used in the binding assay.

Figure 9 shows the specificity of hammerhead ribozymes targeted against flt-1 receptor. Inhibition of the binding of VEGF, urokinase plasminogen activator (UPA) and fibroblast growth factor (FGF) to their corresponding receptors as a function of anti-FLT ribozymes is shown. The sequence and description of the ribozymes used are as described under Figure 7 above. The average of triplicate samples is given; percent inhibition as calculated below.

Figure 10 shows the inhibition of the proliferation of Human aortic endothelial cells (HAEC) mediated by phosphorothicate antisense oligodeoxynucleotides targeted against human KDR receptor RNA. Cell proliferation (O.D. as a function of antisense oligodeoxynucleotide 35 concentration is shown. KDR 21AS represents a 21 nt phosphorothioate antisense oligodeoxynucleotide targeted against KDR RNA. KDR 21 Scram represents a 21 nt

10

15

20

25

phosphorothicate oligodeoxynucleotide having a scrambled sequence. LF represents the lipid carrier Lipofectin.

Figure 11 shows in vitro cleavage of flt-1 RNA by hammerhead ribozymes. A) diagrammatic representation of hammerhead ribozymes targeted against flt-1 RNA. The hammerhead (HH) ribozymes were chemically modified such that the ribozyme consists of ribose residues at five positions; U4 and U7 positions contain $2'-NH_2$ modifications, the remaining nucleotide positions 2'-0-methyl substitutions; four nucleotides at the 5' 10 contains phosphorothioate substitutions. Additionally, the 3' end of the ribozyme contains a 3'-3'linked inverted abasic deoxyribose (designated as 3'-iH). 1358 HH-A and 4229 HH-A contain 3 base-paired stem II 15 1358 HH-B and 4229 HH-B contain 4 base-paired region. stem II region. B) and C) shows in vitro cleavage kinetics of HH ribozymes targeted against sites 1358 and 4229 within the flt-1 RNA.

Figure 12 shows inhibition of human microvascular 20 endothelial cell proliferation mediated by anti-flt-1 hammerhead ribozymes. A) Diagrammatic representation of hammerhead (HH) ribozymes targeted against sites 1358 and 4229 within the the flt-1 RNA. B) Graphical representation of the inhibition of cell proliferation mediated by 1358HH and 4229HH ribozymes.

Figure 13 shows inhibition of human microvascular endothelial cell proliferation mediated by anti-KDR hammerhead ribozymes. The figure is a graphical representation of the inhibition of cell proliferation mediated by hammerhead ribozymes targeted against sites 527, 730, 3702 and 3950 within the KDR RNA. Irrelevant HH RZ is a hammerhead ribozyme targeted to an irrelevant target. All of these ribozymes, including the Irrelevant HH RZ, were chemically modified such that the ribozyme consists of ribose residues at five positions; U4 and U7 positions contain 2'-NH₂ modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions; four

PCT/US96/17480 WO 97/15662

16

nucleotides at the 5' termini contain phosphorothioate substitutions. Additionally, the 3' end of the ribozyme contains a 3'-3' linked inverted abasic deoxyribose (3'-iH).

Figure 14 shows in vitro cleavage of KDR RNA by hammerhead ribozymes. The hammerhead (HH) ribozymes were chemically modified such that the ribozyme consists of ribose residues at five positions; U4 and U7 positions contain 2'-NH2 modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions. Additionally, the 3' end of the ribozyme contains a 3'-3' linked inverted abasic deoxyribose (designated as 3'-iH). 726 HH and 527 HH contain 4 base-paired stem II region. Percent in vitro cleavage kinetics as a function of time of HH ribozymes targeted against sites 527 and 726 within the KDR RNA is shown.

Figure 15 shows in vitro cleavage of KDR RNA by hammerhead ribozymes. The hammerhead (HH) ribozymes were chemically modified such that the ribozyme consists of ribose residues at five positions; U4 and U7 positions contain 2'-NH2 modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions. Additionally, the 3' end of the ribozyme contains a 3'-3' linked inverted abasic deoxyribose (designated as 3'-iH). 25 HH and 3950 HH contain 4 base-paired stem II region. Percentin vitro cleavage kinetics as a function of time of HH ribozymes targeted against sites 3702 and 3950 within the KDR RNA is shown.

Figure 16 shows in vitro cleavage of RNA by hammerhead ribozymes that are targeted to sites that conserved between flt-1 and KDR RNA. The hammerhead (HH) ribozymes were chemically modified such that the ribozyme consists of ribose residues at five positions; U4 and U7 positions contain 2'-NH2 modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions. Additionally, the 3' end of the ribozyme contains a 3'-3' linked inverted abasic deoxyribose (designated as 3'-iH).

17

FLT/KDR-I HH ribozyme was synthesized with either a 4 base-paired or a 3 base-paired stem II region. FLT/KDR-I HH can cleave site 3388 within flt-1 RNA and site 3151 within KDR RNA. Percent *in vitro* cleavage kinetics as a function of time of HH ribozymes targeted against sites 3702 and 3950 within the KDR RNA is shown.

Figure 17 shows inhibition of human microvascular endothelial cell proliferation mediated by anti-KDR and anti-flt-1 hammerhead ribozymes. The figure is a graphical representation of the inhibition of cell prolifera-10 tion mediated by hammerhead ribozymes targeted against sites KDR sites-527, 726 or 3950 or flt-1 site 4229. figure also shows enhanced inhibition of cell proliferation by a combination of flt-1 and KDR hammerhead ribo-15 4229+527, indicates the treatment of cells with both the flt 4229 and the KDR 527 ribozymes. 4229+726, indicates the treatment of cells with both the flt 4229 and the KDR 726 ribozymes. 4229+3950, indicates the treatment of cells with both the flt 4229 and the KDR 3950 VEGF -, indicates the basal level of cell 20 ribozymes. proliferation in the absence of VEGF. Α. indicates catalytically active ribozyme; I, indicates catalytically inactive ribozyme. All of these ribozymes were chemically modified such that the ribozyme consists of residues at five positions; U4 and U7 positions contain 25 $2'-NH_2$ modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions; four nucleotides at the termini contain phosphorothicate substitutions. Additionally, the 3' end of the ribozyme contains a 3'-3'linked inverted abasic deoxyribose (3'-iH). 30

Figure 18 shows the inhibition of VEGF-induced angiogenesis in rat cornea mediated by anti-flt-1 hammerhead ribozyme. All of these ribozymes were chemically modified such that the ribozyme consists of ribose residues at five positions; U4 position contains 2'-C-allyl modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions; four nucleotides at the 5' termini contain

phosphorothicate substitutions. Additionally, the 3' end of the ribozyme contains a 3'-3' linked inverted abasic deoxyribose (3'-iH). A decrease in the Surface Area corresponds to a reduction in angiogenesis. VEGF alone, 5 corresponds to treatment of the cornea with VEGF and no Vehicle alone, corresponds to the treatment of the cornea with the carrier alone and no VEGF. control gives a basal level of Surface Area. Active 4229 HH, corresponds to the treatment of cornea with the flt-1 4229 HH ribozyme in the absence of any VEGF. This control also gives a basal level of Surface Area. Active 4229 HH + VEGF, corresponds to the co-treatment of cornea with the flt-1 4229 HH ribozyme and VEGF. Inactive 4229 HH + VEGF, corresponds to the co-treatment of cornea with a catalytically inactive version of 4229 HH ribozyme and VEGF.

Ribozymes

20

25

35

Ribozymes of this invention block to some extent VEGF-R (specifically flt-1 and flk-1/KDR) production and can be used to treat disease or diagnose such disease. Ribozymes will be delivered to cells in culture, to cells or tissues in animal models of angiogenesis and/or RA and to human cells or tissues ex vivo or in vivo. Ribozyme cleavage of VEGF-R RNAs (specifically RNAs that encode flt-1 and flk-1/KDR) in these systems may alleviate disease symptoms.

Target sites

Targets for useful ribozymes can be determined as disclosed in Draper et al., International PCT Publication No. WO 95/13380, and hereby incorporated by reference herein in totality. Other examples include the following PCT applications which concern inactivation of expression of disease-related genes: WO 95/23225, WO 95/13380, WO 94/02595, incorporated by reference herein. Rather than repeat the guidance provided in those documents here, below are provided specific examples of such methods, not

of ribozyme.

limiting to those in the art. Ribozymes to such targets are designed as described in those applications and synthesized to be tested *in vitro* and *in vivo*, as also described.

The sequence of human and mouse flt-1, KDR and/or flk-1 mRNAs were screened for optimal ribozyme target sites using a computer folding algorithm. Hammerhead or hairpin ribozyme cleavage sites were identified. sites are shown in Tables II to IX (all sequences are 5' to 3' in the tables; X can be any base-paired sequence, the actual sequence is not relevant here). The nucleotide base position is noted in the Tables as that site to be cleaved by the designated type of ribozyme. While mouse and human sequences can be screened and ribozymes thereafter designed, the human targeted sequences are of most 15 However, as discussed in Stinchcomb et al., utility. "Method and Composition for Treatment of Restenosis and Cancer Using Ribozymes," filed May 18, 1994, U.S.S.N. 08/245,466, mouse targeted ribozymes may be useful to test efficacy of action of the ribozyme prior to testing in 20 The nucleotide base position is noted in the

Hammerhead or hairpin ribozymes were designed that could bind and cleave target RNA in a sequence-specific manner. The ribozymes were individually analyzed by computer folding (Jaeger et al., 1989 Proc. Natl. Acad. Sci. USA, 86, 7706) to assess whether the ribozyme sequences fold into the appropriate secondary structure.

Tables as that site to be cleaved by the designated type

Those ribozymes with unfavorable intramolecular interactions between the binding arms and the catalytic core were eliminated from consideration. Varying binding arm lengths can be chosen to optimize activity.

Referring to Figure 6, mRNA is screened for accessible cleavage sites by the method described generally in Draper et al., PCT WO93/23569, hereby incorporated by reference herein. Briefly, DNA oligonucleotides

complementary to potential hammerhead or hairpin ribozyme cleavage sites were synthesized. A polymerase chain reaction is used to generate substrates for T7 polymerase transcription from human and mouse flt-1, KDR and/or flk-1 cDNA clones. Labeled RNA transcripts are synthesized in vitro from the templates. The oligonucleotides and the labeled transcripts were annealed, RNAseH was added and the mixtures were incubated for the designated times at 37°C. Reactions are stopped and RNA separated on sequencing polyacrylamide gels. The percentage of the substrate cleaved is determined by autoradiographic quantitation using a PhosphorImaging system. From these data, hammerhead or hairpin ribozyme sites are chosen as the most accessible.

Ribozymes of the hammerhead or hairpin motif were 15 designed to anneal to various sites in the mRNA message. The binding arms are complementary to the target site sequences described above. The ribozymes were chemically synthesized. The method of synthesis used follows the 20 procedure for normal RNA synthesis as described in Usman 1987 J. Am. Chem. Soc., 109, 7845; Scaringe et al., 1990 Nucleic Acids Res., 18, 5433; and Wincott et al., 1995 Nucleic Acids Res. 23, 2677-2684 and makes use of common nucleic acid protecting and coupling groups, such as dimethoxytrityl at the 5'-end, and phosphora-25 midites at the 3'-end. Small scale synthesis were conducted on a 394 Applied Biosystems, Inc. synthesizer using a modified 2.5 μ mol scale protocol with a 5 min coupling step for alkylsilyl protected nucleotides and 2.5 30 min coupling step for 2'-O-methylated nucleotides. XI outlines the amounts, and the contact times, of the reagents used in the synthesis cycle. A 6.5-fold excess (163 μ L of 0.1 M = 16.3 μ mol) of phosphoramidite and a 24-fold excess of S-ethyl tetrazole (238 μ L of 0.25 M = 59.5 μ mol) relative to polymer-bound 5'-hydroxyl was used 35 in each coupling cycle. Average coupling yields on the 394 Applied Biosystems, Inc. synthesizer, determined by

15

25

colorimetric quantitation of the trityl fractions, were 97.5-99%. Other oligonucleotide synthesis reagents for the 394 Applied Biosystems, Inc. synthesizer: detritylation solution was 2% TCA in methylene chloride (ABI); capping was performed with 16% N-methyl imidazole in THF (ABI) and 10% acetic anhydride/10% 2,6-lutidine in THF oxidation solution was 16.9 mM I_2 , 49 mM pyridine, 9% water in THF (Millipore). B & J Synthesis Grade acetonitrile was used directly from the reagent bottle. S-Ethyl tetrazole solution (0.25 M in acetonitrile) was made up from the solid obtained from American International Chemical, Inc.

Deprotection of the RNA was performed as follows. The polymer-bound oligoribonucleotide, trityl-off, was transferred from the synthesis column to a 4mL glass screw top vial and suspended in a solution of methylamine (MA) at 65 °C for 10 min. After cooling to -20 °C, the supernatant was removed from the polymer support. The support was washed three times with 1.0 mL of EtOH: $MeCN: H_2O/3:1:1$, 20 vortexed and the supernatant was then added to the first supernatant. The combined supernatants, containing the oligoribonucleotide, were dried to a white powder.

The base-deprotected oligoribonucleotide was resuspended in anhydrous TEA \bullet HF/NMP solution (250 μ L of a solution of 1.5mL N-methylpyrrolidinone, 750 μ L TEA and 1.0 mL TEA•3HF to provide a 1.4M HF concentration) and heated to 65°C for 1.5 h. The resulting, fully deprotected, oligomer was quenched with 50 mM TEAB (9 mL) prior to anion exchange desalting.

For anion exchange desalting of the deprotected 30 oligomer, the TEAB solution was loaded onto a Qiagen 500® anion exchange cartridge (Qiagen Inc.) that was prewashed with 50 mM TEAB (10 mL). After washing the loaded cartridge with 50 mM TEAB (10 mL), the RNA was eluted with 2 M TEAB (10 mL) and dried down to a white powder.

Inactive hammerhead ribozymes were synthesized by substituting a U for G_{ϵ} and a U for $A_{1\epsilon}$ (numbering from

22

Hertel, K. J., et al., 1992, <u>Nucleic Acids Res.</u>, 20, 3252).

The average stepwise coupling yields were >98% (Wincott et al., 1995 Nucleic Acids Res. 23, 2677-2684).

Hairpin ribozymes are synthesized in two parts and annealed to reconstruct the active ribozyme (Chowrira and Burke, 1992 Nucleic Acids Res., 20, 2835-2840). Ribozymes are also synthesized from DNA templates using bacteriophage T7 RNA polymerase (Milligan and Uhlenbeck, 1989, Methods Enzymol. 180, 51).

All ribozymes are modified extensively to enhance stability by modification with nuclease resistant groups, for example, 2'-amino, 2'-C-allyl, 2'-flouro, 2'-O-methyl, 2'-H (for a review see Usman and Cedergren, 1992 TIBS 17, 34; Usman et al., 1994 Nucleic Acids Symp. Ser. 31, 163). Ribozymes are purified by gel electrophoresis using general methods or are purified by high pressure liquid chromatography (HPLC; See Usman et al., PCT Publication No. WO95/23225, the totality of which is hereby incorporated herein by reference) and are resuspended in water.

The sequences of the ribozymes that are chemically synthesized, useful in this study, are shown in Tables II to IX. Those in the art will recognize that these sequences are representative only of many more such sequences where the enzymatic portion of the ribozyme (all but the binding arms) is altered to affect activity. Stem-loop IV sequence of hairpin ribozymes listed in for example Table (5'-CACGUUGUG-3') can be altered III (substitution, deletion, and/or insertion) to contain any sequence, provided a minimum of two base-paired stem structure can form. The sequences listed in Tables II to IX may be formed of ribonucleotides or other nucleotides or non-nucleotides. Such ribozymes are equivalent to the ribozymes described specifically in the Tables.

5

10

15

25

Optimizing Ribozyme Activity

Ribozyme activity can be optimized as described by Stinchcomb et al., supra. The details will not be repeated here, but include altering the length of the ribozyme binding arms (stems I and III, see Figure 2c), or chemically synthesizing ribozymes with modifications that prevent their degradation by serum ribonucleases (see Eckstein et al., International Publication No. WO 92/07065; Perrault et al., 1990 Nature 344, 565; Pieken et al., 1991 Science 253, 314; Usman and Cedergren, 1992 Trends in Biochem. Sci. 17, 334; Usman et al., Interna-Publication No. WO 93/15187; Rossi International Publication No. WO 91/03162; Beigelman et al., 1995 J. Biol Chem. in press; as well as Sproat, US Patent No. 5,334,711 which describe various chemical modifications that can be made to the sugar moieties of enzymatic RNA molecules). Modifications which enhance their efficacy in cells, and removal of stem II bases to shorten RNA synthesis times and reduce chemical requirements are desired. (All these publications are hereby incorporated by reference herein).

Sullivan, et al., supra, describes the general methods delivery for οf enzymatic RNA molecules. Ribozymes may be administered to cells by a variety of methods known to those familiar to the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres. For some indications, ribozymes may be directly delivered ex vivo to cells or tissues with or without the aforementioned vehicles. Alternatively, the RNA/vehicle combination is locally delivered by direct injection or by use of a catheter, infusion pump or stent. Other routes of delivery include, but are not limited to, intravascular, intramuscular, subcutaneous or injection, aerosol inhalation, oral (tablet or pill form), topical, systemic, ocular, intraperitoneal and/or intra-

15

20

thecal delivery. More detailed descriptions of ribozyme delivery and administration are provided in Sullivan et al., supra and Draper et al., supra which have been incorporated by reference herein.

Another means of accumulating high concentrations of 5 a ribozyme(s) within cells is to incorporate the ribozymeencoding sequences into a DNA or RNA expression vector. Transcription of the ribozyme sequences are driven from a promoter for eukaryotic RNA polymerase I (pol I), RNA polymerase II (pol II), or RNA polymerase III (pol III). 10 Transcripts from pol II or pol III promoters will be expressed at high levels in all cells; the levels of a given pol II promoter in a given cell type will depend on the nature of the gene regulatory sequences (enhancers, silencers, etc.) present nearby. Prokaryotic RNA polymer-15 ase promoters are also used, providing that the prokaryotic RNA polymerase enzyme is expressed in the appropriate cells (Elroy-Stein and Moss, 1990 Proc. Natl. Acad. Sci. U S A, 87, 6743-7; Gao and Huang 1993 Nucleic Acids Res., 21, 2867-72; Lieber et al., 1993 Methods Enzymol., 47-66; Zhou et al., 1990 Mol. Cell. Biol., 10, 4529-37; Thompson et al., 1995 supra). Several investigators have demonstrated that ribozymes expressed from such promoters can function in mammalian cells (e.g. Kashani-Sabet et 25 al., 1992 Antisense Res. Dev., 2, 3-15; Ojwang et al., 1992 Proc. Natl. Acad. Sci. U S A, 89, 10802-6; Chen et al., 1992 Nucleic Acids Res., 20, 4581-9; Yu et al., 1993 Proc. Natl. Acad. Sci. U S A, 90, 6340-4; L'Huillier et al., 1992 EMBO J. 11, 4411-8; Lisziewicz et al., 1993 Proc. Natl. Acad. Sci. U. S. A., 90, 8000-4; Thompson et 30 al., 1995 Nucleic Acids Res. 23, 2259). The above ribozyme transcription units can be incorporated into a variety of vectors for introduction into mammalian cells, including but not restricted to, plasmid DNA vectors, 35 viral DNA vectors (such as adenovirus or adeno-associated virus vectors), or viral RNA vectors (such as retroviral

or alphavirus vectors).

25

In a preferred embodiment of the invention, transcription unit expressing a ribozyme that cleaves RNAs that encode flt-1, KDR and/or flk-1 are inserted into a plasmid DNA vector or an adenovirus or adeno-associated virus DNA viral vector or a retroviral RNA vector. Viral vectors have been used to transfer genes and lead to either transient or long term gene expression (Zabner et al., 1993 <u>Cell</u> 75, 207; Carter, 1992 <u>Curr. Opi. Biotech.</u> The adenovirus, AAV or retroviral vector is 3, 533). delivered as recombinant viral particles. The DNA may be delivered alone or complexed with vehicles (as described for RNA above). The recombinant adenovirus or AAV or retroviral particles are locally administered to the site of treatment, e.g., through incubation or inhalation in vivo or by direct application to cells or tissues ex 15 vivo. Retroviral vectors have also been used to express ribozymes in mammalian cells (Ojwang et al., 1992 supra; Thompson et al., 1995 supra).

acid-based therapeutic targets by several criteria. The interaction between VEGF and VEGF-R is well-established. Efficacy can be tested in well-defined and predictive animal models. Finally, the disease conditions are serious and current therapies are inadequate. Whereas protein-based therapies would inhibit VEGF activity nucleic acid-based therapy provides a direct and elegant approach to directly modulate flt-1, KDR and/or flk-1 expression.

Because flt-1 and KDR mRNAs are highly homologous in certain regions, some ribozyme target sites are also homologous (see Table X). In this case, a single ribozyme will target both flt-1 and KDR mRNAs. At partially homologous sites, a single ribozyme can sometimes be designed to accomodate a site on both mRNAs by including G/U basepairing. For example, if there is a G present in a ribozyme target site in KDR mRNA at the same position there is an A in the flt-1 ribozyme target site, the

20

25

ribozyme can be synthesized with a U at the complementary position and it will bind both to sites. The advantage of one ribozyme that targets both VEGF-R mRNAs is clear, especially in cases where both VEGF receptors may con-5 tribute to the progression of angiogenesis in the disease state.

"Angiogenesis" refers to formation of new blood vessels which is an essential process in reproduction, development and wound repair. "Tumor angiogenesis" refers to the induction of the growth of blood vessels from surrounding tissue into a solid tumor. Tumor growth and tumor metastasis are dependent on angiogenesis (for a review see Folkman, 1985 supra; Folkman 1990 J. Natl. Cancer Inst., 82, 4; Folkman and Shing, 1992 J. Biol. 15 Chem. 267, 10931).

Angiogenesis plays an important role diseases such as arthritis wherein new blood vessels have been shown to invade the joints and degrade cartilage (Folkman and Shing, supra).

"Retinopathy" refers to inflammation of the retina and/or degenerative condition of the retina which may lead to occlusion of the retina and eventual blindness. "diabetic retinopathy" angiogenesis causes the capillaries in the retina to invade the vitreous resulting in bleeding and blindness which is also seen in neonatal retinopathy (for a review see Folkman, 1985 supra; Folkman 1990 supra; Folkman and Shing, 1992 supra).

Example 1: flt-1, KDR and/or flk-1 ribozymes

By engineering ribozyme motifs applicant has designed several ribozymes directed against flt-1, KDR and/or flk-1 encoded mRNA sequences. These ribozymes were synthesized with modifications that improve their nuclease resistance (Beigelman et al., 1995 J Biol. Chem. 270, 25702) and enhance their activity in cells. The ability of ribozymes to cleave target sequences in vitro was evaluated essentially as described in Thompson et al., PCT Publication

No. WO 93/23057; Draper et al., PCT Publication No. WO 95/04818.

Example 2: Effect of ribozymes on the binding of VEGF to flt-1, KDR and/or flk-1 receptors

Several common human cell lines are available that express endogenous flt-1, KDR and/or flk-1. flt-1, KDR and/or flk-1 can be detected easily with monoclonal antibodies. Use of appropriate fluorescent reagents and fluorescence-activated cell-sorting (FACS) will permit direct quantitation of surface flt-1, KDR and/or flk-1 on a cell-by-cell basis. Active ribozymes are expected to directly reduce flt-1, KDR and/or flk-1 expression and thereby reduce VEGF binding to the cells. In this example, human umbelical cord microvascular endothelial cells were used.

Cell Preparation:

Plates are coated with 1.5% gelatin and allowed to stand for one hour. Cells (e.g., microvascular endothelial cells derived from human umbilical cord vein) are plated at 20,000 cells/well (24 well plate) in 200 ml growth media and incubated overnight (~ 1 doubling) to yield ~40,000 cells (75-80% confluent).

Ribozyme treatment:

Media is removed from cells and the cells are washed two times with 300 ml 1X PBS: Ca²⁺: Mg²⁺ mixture. A complex of 200-500 nM ribozyme and LipofectAMINE[®] (3:1 lipid: phosphate ratio) in 200 ml OptiMEM[®] (5% FBS) was added to the cells. The cells are incubated for 6 hr (equivalent to 2-3 VEGF-R turnovers).

30 125 I VEGF binding assay:

The assay is carried out on ice to inhibit internalization of VEGF during the experiment. The media containing the ribozyme is removed from the cells and the cells

are washed twice with with 300 ml 1X PBS: Ca²⁺: Mg²⁺ mixture containing 1% BSA. Appropriate ¹²⁵I VEGF solution (100,000 cpm/well, +/- 10 X cold 1X PBS, 1% BSA) was applied to the cells. The cells are incubated on ice for 1 h. ¹²⁵I VEGF-containing solution is removed and the cells are washed three times with with 300 ml 1X PBS: Ca²⁺: Mg²⁺ mixture containing 1% BSA. To each well 300 ml of 100 mM Tris-HCl, pH 8.0, 0.5% Triton X-100 was added and the the mixture was incubated for 2 min. The ¹²⁵I VEGF-binding was quantitated using standard scintillation counting techniques. Percent inhibition was calculated as follows:

Percent Inhibition =

cpm 125I VEGF bound by the ribozyme-treated samples x 100
cpm 125I VEGF bound by the Control sample

15 Example 3: Effect of hammerhead ribozymes targeted against flt-1 receptor on the binding of VEGF

Hammerhead ribozymes targeted to twenty sites within flt-1 RNA were synthesized as described above. Sequence of the ribozymes used are shown in Table II; the length of stem II region is 3 bp. The hammerhead ribozymes were chemically modified such that the ribozyme consists of ribose residues at five positions; U4 and U7 positions contain 2'-NH₂ modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions; four nucleotides at the 5' terminus contains phosphorothicate substitutions. Additionally, 3' end of the ribozyme contains a 3'-3' linked inverted abasic ribose.

Referring to Figure 7, the effect of hammerhead ribozymes targeted against flt-1 receptor on the binding of VEGF to flt-1 on the surface of human microvascular endothelial cells is shown. The majority of the ribozymes tested were able to inhibit the expression of flt-1 and thereby were able to inhibit the binding of VEGF.

In order to determine the specificity of ribozymes targeted against flt-1 RNA, the effect of five anti-flt-1 ribozymes on the binding of VEGF, UPA (urokinase plasmino-

gen activator) and FGF (fibroblast growth factor) to their corresponding receptors were assayed. As shown in Figure 9, there was significant inhibition of VEGF binding to its receptors on cells treated with anti-flt-1 ribozymes. 5 There was no specific inhibition of the binding of UPA and FGF to their corresponding receptors. These data strongly suggest that anti-flt-1 ribozymes specifically cleave flt-1 RNA and not RNAs encoding the receptors for UPA and FGF, resulting in the inhibition of flt-1 receptor expression on the surface of the cells. Thus the ribozymes are responsible for the inhibition of VEGF binding but not the binding of UPA and FGF.

Example 4: Effect of hammerhead ribozymes targeted against KDR receptor on the binding of VEGF

Hammerhead ribozymes targeted to twenty one sites: 15 within KDR RNA were synthesized as described above. Sequence of the ribozymes used are shown in Table IV; the length of stem II region is 3 bp. The hammerhead ribo- t zymes were chemically modified such that the ribozyme consists of ribose residues at five positions; U4 and U7___ positions contain $2'-NH_2$ modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions; four nucleotides at the 5' terminus contains phosphorothioate substitutions. Additionally, the 3' end of the 25 ribozyme contains a 3'-3' linked inverted abasic deoxyribose.

Referring to Figure 8, the effect of hammerhead ribozymes targeted against KDR receptor on the binding of VEGF to KDR on the surface of human microvascular endothelial cells is shown. A majority of the ribozymes were able to inhibit the expression of KDR and thereby were able to inhibit the binding of VEGF. As a control, the cells were treated with a ribozyme that is not targeted towards KDR RNA (irrel. RZ); there was no specific inhibition of VEGF binding. The results from 35 this control experiment strongly suggest that the inhibi-

30

tion of VEGF binding observed with anti-KDR ribozymes is a ribozyme-mediated inhibition.

Example 5: Effect of ribozymes targeted against VEGF receptors on cell proliferation

5 Cell Preparation:

10

24-well plates are coated with 1.5% gelatin (porcine skin 300 bloom). After 1 hr, excess gelatin is washed off of the plate. Microvascular endothelial cells are plated at 5,000 cells/well (24 well plate) in 200 ml growth media. The cells are allowed to grow for ~ 18 hr (~ 1 doubling) to yield ~10,000 cells (25-30% confluent).

Ribozyme treatment:

Media is removed from the cells, and the cells are washed two times with 300 ml 1X PBS: Ca^{2+} : Mg^{2+} mixture.

- For anti-flt-1 HH ribozyme experiment (Figure 12) a complex of 500 nM ribozyme; 15 mM LFA (3:1 lipid:phosphate ratio) in 200 ml OptiMEM (5% FCS) media was added to the cells. Incubation of cells is carried out for 6 hr (equivalent to 2-3 VEGF receptor turnovers).
- For anti-KDR HH ribozyme experiment (Figure 13) a complex of 200 nM ribozyme; 5.25 mM LFA (3:1 lipid: phosphate ratio) in 200 ml OptiMEM (5% FCS) media was added to the cells. Incubation of cells is carried out for 3 hr.

25 <u>Proliferation:</u>

After three or six hours, the media is removed from the cells and the cells are washed with 300 ml 1X PBS: Ca²⁺: Mg²⁺ mixture. Maintenance media (contains dialyzed 10% FBS) +/- VEGF or basic FGF at 10 ng/ml is added to the cells. The cells are incubated for 48 or 72 h. The cells are trypsinized and counted (Coulter counter). Trypan blue is added on one well of each treatment as control.

As shown in Figure 12B, VEGF and basic FGF can stimulate human microvascular endothelial cell proliferation. However, treatment of cells with 1358 HH or 4229 HH ribozymes, targeted against flt-1 mRNA, results in a significant decrease in the ability of VEGF to stimulate endothelial cell proliferation. These ribozymes do not inhibit the FGF-mediated stimulation of endothelial cell proliferation.

Human microvascular endothalial cells were also treated with hammerhead ribozymes targeted against sites 527, 730, 3702 or 3950 within the KDR mRNA. As shown in Figure 13, all four ribozymes caused significant inhibition of VEGF-mediated induction of cell proliferation. No significant inhibition of cell proliferation was observed when the cells were treated with a hammerhead ribozyme targeted to an irrelevant RNA. Additionally, none of the ribozymes inhibited FGF-mediated stimulation of cell proliferation.

These results strongly suggest that hammerhead ribozymes targeted against either flt-1 or KDR mRNA can specifically inhibit VEGF-mediated induction of endothelial cell proliferation.

Example 6: Effect of antisense oligonucleotides targeted against VEGF receptors on cell proliferation (colorimetric assay)

Following are some of the reagents used in the proliferation assay:

<u>Cells:</u> Human aortic endothelial cells (HAEC) from Clonetics[®]. Cells at early passage are preferably used.

30 <u>Uptake Medium:</u> EBM (from Clonetics®);1% L-Glutamine;20 mM Hepes; No serum; No antibiotics.

Growth Medium: EGM (from Clonetics $^{\odot}$);FBS to 20%;1% L-Glutamine;20 mM Hepes.

Cell Plating: 96-well tissue culture plates are coated with 0.2% gelatin (50 ml/well). The gelatin is incubated in the wells at room temperature for 15-30

minutes. The gelatin is removed by aspiration and the wells are washed with PBS:Ca²⁺: Mg²⁺ mixture. PBS mixture is left in the wells until cells are ready to be added. HAEC cells were detached by trypsin treatment and resuspended at 1.25 x 10⁴/ml in growth medium. PBS is removed from plates and 200 ml of cells (i.e. 2.5 x 10³ cells/well) are added to each well. The cells are allowed to grow for 48 hours before the proliferation assay.

Assay: Growth medium is removed from the wells. The cells are washed twice with PBS:Ca2+: Mg2+ mixture without antibiotics. A formulation of lipid/antisense oligonucleotide (antisense oligonucleotide is used here as a non-limiting example) complex is added to each well (100 ml/well) in uptake medium. The cells are incubated for 2-3 hours at 37°C in CO2 incubator. After uptake, 100 15 ml/well of growth medium is added (gives final FBS concentration of 10%). After approximately 72 hours, 40 ml MTS® stock solution (made as described by manufacturer) was added to each well and incubated at 37°C for 1-3 hours, depending on the color development. (For this 20 assay, 2 hours was sufficient). The intensity of color formation was determined on a plate reader at 490 nM.

Phosphorothioate-substituted antisense oligodeoxynucleotides were custom synthesized by The Midland Certified Reagent Company[®], Midland, Texas. Following non-limiting antisense oligodeoxynucleotides targeted against KDR RNA were used in the proliferation assay:

KDR 21 AS: 5'-GCA GCA CCT TGC TCT CCA TCC-3'

SCRAMBLED CONTROL: 5'-CTG CCA ACT TCC CAT GCC TGC-3'

As shown in Figure 10, proliferation of HAEC cells are specifically inhibited by increasing concentrations of the phosphorothicate anti-KDR-antisense oligodeoxynucleotide. The scrambled antisense oligonucleotide is not expected to bind the KDR RNA and therefore is not expected to inhibit KDR expression. As expected, there is no detectable inhibition of proliferation of HAEC cells

treated with a phosphorothicate antisense oligonucleotide with scrambled sequence.

Example 7: In vitro cleavage of flt-1 RNA by hammerhead ribozymes

Referring to Figure 11A, hammerhead ribozymes (HH) targeted against sites 1358 and 4229 within the flt-1 RNA were synthesized as described above.

RNA cleavage assay in vitro:

Substrate RNA was 5' end-labeled using [g-32P] ATP and 10 T4 polynucleotide kinase (US Biochemicals). Cleavage reactions were carried out under ribozyme "excess" conditions. Trace amount (s 1 nM) of 5' end-labeled substrate and 40 nM unlabeled ribozyme were denatured and renatured separately by heating to 90°C for 2 min and snap-cooling—

- on ice for 10-15 min. The ribozyme and substrate were incubated, separately, at 37°C for 10 min in a buffer containing 50 mM Tris-HCl and 10 mM MgCl₂. The reaction was initiated by mixing the ribozyme and substrate solutions and incubating at 37°C. Aliquots of 5 ml are taken
- at regular intervals of time and the reaction is quenched by mixing with equal volume of 2X formamide stop mix. The samples are resolved on 20 % denaturing polyacrylamide gels. The results were quantified and percentage of target RNA cleaved is plotted as a function of time.
- Referring to Figure 11B and 11C, hammerhead ribozymes targeted against sites 1358 and 4229 within the flt-1 RNA are capable of cleaving target RNA efficiently in vitro.

Example 8: In vitro cleavage of KDR RNA by hammerhead ribozymes

In this non-limiting example, hammerhead ribozymes targeted against sites 726, 527, 3702 and 3950 within KDR RNA were synthesized as described above. RNA cleavage reactions were carried out in vitro essentially as described under Example 7.

Referring to Figures 14 and 15, all four ribozymes were able to cleave their cognate target RNA efficiently in a sequence-specific manner.

Example 9: In vitro cleavage of RNA by hammerhead ribo-5 zymes targeted against cleavage sites that are homologous between KDR and flt-1 mRNA

Because flt-1 and KDR mRNAs are highly homologous in certain regions, some ribozyme target sites are also homologous (see Table X). In this case, a single ribozyme 10 will target both flt-1 and KDR mRNAs. Hammerhead ribozyme (FLT/KDR-I) targeted against one of the homologous sites between flt-1 and KDR (flt-1 site 3388 and KDR site 3151) was synthesized as described above. Ribozymes with either a 3 bp stem II or a 4 bp stem II were synthesized. 15 RNA cleavage reactions were carried out in vitro essentially as described under Example 7.

Referring to Figure 16, FLT/KDR-I ribozyme with either a 3 or a 4 bp stem II was able to cleave its target RNA efficiently in vitro.

20 Example 10: Effect of multiple ribozymes targeted against both flt-1 and KDR RNA on cell proliferation

Since both flt-1 and KDR receptors of VEGF are involved in angiogenesis, the inhibition of the expression of both of these genes may be an effective approach to 25 inhibit angiogenesis.

Human microvascular endothalial cells were treated with hammerhead ribozymes targeted against sites flt-1 4229 alone, KDR 527 alone, KDR 726 alone, KDR 3950 alone, flt-1 4229 + KDR 527, flt-1 4229 + KDR 726 or flt-1 4229 + KDR 3950. As shown in Figure 17, all the combinations of active ribozymes (A) caused significant inhibition of VEGF-mediated induction of cell proliferation. significant inhibition of cell proliferation was observed when the cells were treated with a catalytically inactive 35 (I) hammerhead ribozymes. Additionally, cells treated

35

with ribozymes targeted against both flt-1 and KDR RNAs-flt-1 4229 + KDR 527; flt-1 4229 + KDR 726; flt-1 4229 + KDR 3950, were able to cause a greater inhibition of VEGF-mediated induction of cell proliferation when compared with individual ribozymes targeted against either flt-1 or KDR RNA (see flt-1 4229 alone; KDR 527 alone; KDR 726 alone; KDR 3950 alone). This strongly suggests that treatment of cells with multiple ribozymes may be a more effective means of inhibition of gene expression.

10 Animal Models

There are several animal models in which anti-angiogenesis effect of nucleic acids of the present invention, such as ribozymes, directed against VEGF-R mRNAs can be tested. Typically a corneal model has been used to study angiogenesis in rat and rabbit since recruitment of vessels can easily be followed in this normally avascular tissue (Pandey et al., 1995 Science 268: 567-569). In these models, a small Teflon or Hydron disk pretreated with an angiogenesis factor (e.g. bFGF or VEGF) is inserted into a pocket surgically created in the 20 Angiogenesis is monitored 3 to 5 days later. Ribozymes directed against VEGF-R mRNAs would be delivered in the disk as well, or dropwise to the eye over the time course of the experiment. In another eye model, hypoxia has been shown to cause both increased expression of VEGF and neovascularization in the retina (Pierce et al., 1995 Proc. Natl. Acad. Sci. USA. 92: 905-909; Shweiki et al., 1992 J. Clin. Invest. 91: 2235-2243).

In human glioblastomas, it has been shown that VEGF is at least partially responsible for tumor angiogenesis (Plate et al., 1992 Nature 359, 845). Animal models have been developed in which glioblastoma cells are implanted subcutaneously into nude mice and the progress of tumor growth and angiogenesism is studied (Kim et al., 1993 supra; Millauer et al., 1994 supra).

36

Another animal model that addresses neovascularization involves Matrigel, an extract of basement membrane that becomes a solid gel when injected subcutaneously (Passaniti et al., 1992 Lab. Invest. 67: 519-528). When the Matrigel is supplemented with angiogenesis factors such as VEGF, vessels grow into the Matrigel over a period of 3 to 5 days and angiogenesis can be assessed. Again, ribozymes directed against VEGF-R mRNAs would be delivered in the Matrigel.

Several animal models exist for screening of anti-10 angiogenic agents. These include corneal vessel formation following corneal injury (Burger et al., 1985 Cornea 4: 35-41; Lepri, et al., 1994 J. Ocular Pharmacol. 10: 280; Ormerod et al., 1990 Am. J. Pathol. 137: 1243-1252) or intracorneal growth factor implant (Grant et al., 1993 15 Diabetologia 36: 282-291; Pandey et al. 1995 supra; Zieche et al., 1992 Lab. Invest. 67: 711-715), vessel growth into Matrigel matrix containing growth factors (Passaniti et al., 1992 supra), female reproductive organ neovasculari-20 zation following hormonal manipulation (Shweiki et al., 1993 Clin. Invest. 91: 2235-2243), several models involving inhibition of tumor growth in highly vascularized solid tumors (O'Reilly et al., 1994 Cell 79: 315-328; Senger et al., 1993 Cancer and Metas. Rev. 12: 303-324; 25 Takahasi et al., 1994 Cancer Res. 54: 4233-4237; Kim et 1993 supra), and transient hypoxia-induced neovascularization in the mouse retina (Pierce et al., 1995 Proc. Natl. Acad. Sci. USA. 92: 905-909).

The cornea model, described in Pandey et al. supra, is the most common and well characterized anti-angiogenic agent efficacy screening model. This model involves an avascular tissue into which vessels are recruited by a stimulating agent (growth factor, thermal or alkalai burn, endotoxin). The corneal model would utilize the intrastromal corneal implantation of a Teflon pellet soaked in a VEGF-Hydron solution to recruit blood vessels toward the pellet which can be quantitated using standard microscopic

37

and image analysis techniques. To evaluate their antiangiogenic efficacy, ribozymes are applied topically to the eye or bound within Hydron on the Teflon pellet itself. This avascular cornea as well as the Matrigel (see below) provide for low background assays. While the corneal model has been performed extensively in the rabbit, studies in the rat have also been conducted.

The mouse model (Passaniti et al., supra) is a non-tissue model which utilizes Matrigel, an extract of basement membrane (Kleinman et al., 1986) or Millipore® 10 filter disk, which can be impregnated with growth factors and anti-angiogenic agents in a liquid form prior to Upon subcutaneous administration at body injection. temperature, the Matrigel or $Millipore^{\oplus}$ filter disk forms VEGF embedded in the Matrigel or 15 a solid implant. Millipore® filter disk would be used to recruit vessels within the matrix of the Matrigel or Millipore® filter disk which can be processed histologically for endothelial cell specific vWF (factor VIII antigen) immunohistochemistry, Trichrome-Masson stain, or hemoglobin content. Like the cornea, the Matrigel or Millipore® filter disk are avascular; however, it is not tissue. In the Matrigel or Millipore® filter disk model, ribozymes are administered within the matrix of the Matrigel or Millipore® filter disk to test their anti-angiogenic efficacy. Thus, 25 delivery issues in this model, as with delivery of ribozymes by Hydron-coated Teflon pellets in the rat cornea model, may be less problematic due to the homogeneous presence of the ribozyme within the respective matrix.

These models offer a distinct advantage over several other angiogenic models listed previously. The ability to use VEGF as a pro-angiogenic stimulus in both models is highly desirable since ribozymes will target only VEGFr mRNA. In other words, the involvement of other non-specific types of stimuli in the cornea and Matrigel models is not advantageous from the standpoint of understanding the pharmacologic mechanism by which the

anti-VEGFr mRNA ribozymes produce their effects. In addition, the models will allow for testing the specificity of the anti-VEGFr mRNA ribozymes by using either a- or bFGF as a pro-angiogenic factor. Vessel recruitment using FGF should not be affected in either model by anti-VEGFr mRNA ribozymes. Other models of angiogenesis including vessel formation in the female reproductive system using hormonal manipulation (Shweiki et al., 1993 supra); a variety of vascular solid tumor models which involve indirect correlations with angiogenesis (O'Reilly et al., 1994 supra; Senger et al., 1993 supra; Takahasi et al., 1994 supra; Kim et al., 1993 supra); and retinal neovascularization following transient hypoxia (Pierce et al., 1995 supra) were not selected for efficacy screening due to their 15 non-specific nature, although there is a correlation between VEGF and angiogenesis in these models.

Other model systems to study tumor angiogenesis is reviewed by Folkman, 1985 Adv. Cancer. Res.. 43, 175.

flt-1, KDR and/or flk-1 protein levels can be measured clinically or experimentally by FACS analysis. flt-1, KDR and/or flk-1 encoded mRNA levels will be assessed by Northern analysis, RNase-protection, primer extension analysis and/or quantitative RT-PCR. Ribozymes that block flt-1, KDR and/or flk-1 protein encoding mRNAs and therefore result in decreased levels of flt-1, KDR 25 and/or flk-1 activity by more than 20% in vitro will be identified.

Ribozymes and/or genes encoding them are delivered by either free delivery, liposome delivery, cationic lipid delivery, adeno-associated virus vector delivery, adenovirus vector delivery, retrovirus vector delivery or plasmid vector delivery in these animal model experiments (see above).

Patients can be treated by locally administering nucleic acids targeted against VEGF-R by direct injection. Routes of administration may include, but are not limited to, intravascular, intramuscular, subcutaneous,

articular, aerosol inhalation, oral (tablet, capsule or pill form), topical, systemic, ocular, intraperitoneal and/or intrathecal delivery.

Example 11: Ribozyme-mediated inhibition of angiogenesis in vivo

The purpose of this study was to assess the antiangiogenic activity of hammerhead ribozymes targeted against flt-1 4229 site in the rat cornea model of VEGF induced angiogenesis (see above). These ribozymes have either active or inactive catalytic core and either bind 10 and cleave or just bind to VEGF-R mRNA of the flt-1 subtype. The active ribozymes, that are able to bind and cleave the target RNA, have been shown to inhibit (125I-labeled) VEGF binding in cultured endothelial cells and produce a dose-dependent decrease in VEGF induced 15 endothelial cell proliferation in these cells Examples 3-5 above). The catalytically inactive forms of these ribozymes, wherein the ribozymes can only bind to the RNA but cannot catalyze RNA cleavage, fail to show 20 these characteristics. The ribozymes and VEGF were co-delivered using the filter disk method: Nitrocellulose filter disks (Millipore®) of 0.057 diameter were immersed in appropriate solutions and were surgically implanted in rat cornea as described by Pandey et al., supra. delivery method has been shown to deliver rhodamine-25 labeled free ribozyme to scleral cells and, likelihood cells of the pericorneal vascular Since the active ribozymes show cell culture efficacy and can be delivered to the target site using the disk method, it is essential that these ribozymes be assessed for in vivo anti-angiogenic activity.

The stimulus for angiogenesis in this study was the treatment of the filter disk with 30 mM VEGF which is implanted within the cornea's stroma. This dose yields reproducible neovascularization stemming from the pericorneal vascular plexus growing toward the disk in a

dose-response study 5 days following implant. Filter disks treated only with the vehicle for VEGF show no angiogenic response. The ribozymes was co-adminstered with VEGF on a disk in two different ribozyme concentrations. One concern with the simultaneous administration is that the ribozymes will not be able to inhibit angiogenesis since VEGF receptors can be stimulated. However, we have observed that in low VEGF doses, the neovascular response reverts to normal suggesting that the VEGF stimulus is essential for maintaining the angiogenic response. Blocking the production of VEGF receptors using simultaneous administration of anti-VEGF-R mRNA ribozymes could attenuate the normal neovascularization induced by the filter disk treated with VEGF.

15 Materials and Methods:

- 1. Stock hammerhead ribozyme solutions:
 - a. flt-1 4229 (786 μ M) Active
 - b. flt-1 4229 (736 μ M) Inactive

2. Experimental solutions/groups:

20	Group 1	Solution 1	Control VEGF solution: 30 μM in
			82mM Tris base
	Group 2	Solution 2	flt-1 4229 (1 $\mu g/\mu L$) in 30 μM
			VEGF/82 mM Tris base
	Group 3	Solution 3	flt-1 4229 (10 $\mu g/\mu L$) in 30 μM
25			VEGF/82 mM Tris base
	Group 4	Solution 4	No VEGF, flt-1 4229 (10 μ g/ μ L)
			in 82 mM Tris base
	Group 5	Solution 5	No VEGF, No ribozyme in 82 mM
			Tris base

30 10 eyes per group, 5 animals (Since they have similar molecular weights, the molar concentrations should be essentially similar).

Each solution (VEGF and RIBOZYMES) were prepared as a 2X solution for 1:1 mixing for final concentrations

above, with the exception of solution 1 in which VEGF was 2X and diluted with ribozyme diluent (sterile water).

3. <u>VEGF Solutions</u>

The 2X VEGF solution (60 μ M) was prepared from a stock of 0.82 μ g/ μ L in 50 mM Tris base. 200 μ L of VEGF stock was concentrated by speed vac to a final volume of 60.8 μ L, for a final concentration of 2.7 μ g/ μ L or 60 μ M. Six 10 μ L aliquots was prepared for daily mixing. 2X solutions for VEGF and Ribozyme was stored at 4°C until 0 the day of the surgery. Solutions were mixed for each day of surgery. Original 2X solutions was prepared on the day before the first day of the surgery.

4. <u>Surgical Solutions</u>:

Anesthesia:

stock ketamine hydrochloride 100 mg/mL stock xylazine hydrochloride 20 mg/mL stock acepromazine 10 mg/mL

Final anesthesia solution: 50 mg/mL ketamine, 10 mg/mL xylazine, and 0.5 mg/mL acepromazine 5% povidone iodine for opthalmic surgical wash 2% lidocaine (sterile) for opthalmic administration (2 drops per eye) sterile 0.9% NaCl for opthalmic irrigation

5. <u>Surgical Methods:</u>

Standard surgical procedure as described in Pandey et al., supra. Filter disks were incubated in 1 μ L of each solution for approximately 30 minutes prior to implantation.

5. Experimental Protocol:

The animal cornea were treated with the treatment groups as described above. Animals were allowed to recover for 5 days after treatment with daily observation (scoring 0 - 3). On the fifth day animals were euthanized and

42

digital images of each eye was obtained for quantitaion using Image Pro Plus. Quantitated neovascular surface area were analyzed by ANOVA followed by two post-hoc tests including Dunnets and Tukey-Kramer tests for significance at the 95% confidence level. Dunnets provide information on the significance between the differences within the means of treatments vs. controls while Tukey-Kramer provide information on the significance of differences within the means of each group.

Results are graphically represented in Figure 18. As shown in the figure, flt-1 4229 active hammerhead ribozyme at both concentrations was effective at inhibiting angiogenesis while the inactive ribozyme did not show any significant reduction in angiogenesis. A statistically signifiant reduction in neovascular surface area was observed only with active ribozymes. This result clearly shows that the ribozymes are capable of significantly inhibiting angiogenesis in vivo. Specifically, the mechanism of inhibition appears to be by the binding and cleavage of target RNA by ribozymes.

Diagnostic uses

Ribozymes of this invention may be used as diagnostic tools to examine genetic drift and mutations within diseased cells or to detect the presence of flt-1, KDR and/or flk-1 RNA in a cell. The close relationship between ribozyme activity and the structure of the target RNA allows the detection of mutations in any region of the molecule which alters the base-pairing and dimensional structure of the target RNA. By using multiple ribozymes described in this invention, one may map nucleotide changes which are important structure and function in vitro, as well as in cells and tissues. Cleavage of target RNAs with ribozymes may be used to inhibit gene expression and define the role (essentially) of specified gene products in the progression of disease. In this manner, other genetic targets

35

10

15

20

may be defined as important mediators of the disease. These experiments will lead to better treatment of the disease progression by affording the possibility of combinational therapies (e.g., multiple ribozymes targeted to different genes, ribozymes coupled with known small molecule inhibitors, or intermittent treatment with combinations of ribozymes and/or other chemical or biological molecules). Other in vitro uses of ribozymes of this invention are well known in the art, and include detection of the presence of mRNAs associated with flt-1, KDR and/or flk-1 related condition. Such RNA is detected by determining the presence of a cleavage product after treatment with a ribozyme using standard methodology.

In a specific example, ribozymes which can cleave only wild-type or mutant forms of the target RNA are used 15 for the assay. The first ribozyme is used to identify wild-type RNA present in the sample and the second ribozyme will be used to identify mutant RNA in the sample. As reaction controls, synthetic substrates of both wildtype and mutant RNA will be cleaved by both ribozymes to 20 demonstrate the relative ribozyme efficiencies in the reactions and the absence of cleavage of the "nontargeted" RNA species. The cleavage products from the synthetic substrates will also serve to generate size markers for the analysis of wild-type and mutant RNAs in the sample population. Thus each analysis will require two ribozymes, two substrates and one unknown sample which will be combined into six reactions. The presence of cleavage products will be determined using an RNAse protection assay so that full-length and cleavage fragments 30 of each RNA can be analyzed in one lane of a polyacryl-It is not absolutely required to quantify the amide gel. results to gain insight into the expression of mutant RNAs and putative risk of the desired phenotypic changes in 35 target cells. The expression of mRNA whose protein product is implicated in the development of the phenotype (i.e., flt-1, KDR and/or flk-1) is adequate to establish

risk. If probes of comparable specific activity are used for both transcripts, then a qualitative comparison of RNA levels will be adequate and will decrease the cost of the initial diagnosis. Higher mutant form to wild-type ratios will be correlated with higher risk whether RNA levels are compared qualitatively or quantitatively.

Other embodiments are within the following claims.

<u>Table I</u>

Characteristics of Ribozymes

Group I Introns

Size: ~200 to >1000 nucleotides

5 Requires a U in the target sequence immediately 5' of the cleavage site.

Binds 4-6 nucleotides at 5' side of cleavage site.

Over 75 known members of this class. Found in Tetrahymena thermophila rRNA, fungal mitochondria, chloroplasts, phage

10 T4, blue-green algae, and others.

RNAseP RNA (M1 RNA)

Size: ~290 to 400 nucleotides

RNA portion of a ribonucleoprotein enzyme. Cleaves tRNA precursors to form mature tRNA.

15 Roughly 10 known members of this group all are bacterial in origin.

Hammerhead Ribozyme

Size: ~13 to 40 nucleotides.

Requires the target sequence UH immediately 5' of the 20 cleavage site.

Binds a variable number of nucleotides on both sides of the cleavage site.

14 known members of this class. Found in a number of plant pathogens (virusoids) that use RNA as the infectious

25 agent (Figure 1 and 2)

Hairpin Ribozyme

Size: ~50 nucleotides.

Requires the target sequence GUC immediately 3' of the cleavage site.

30 Binds 4-6 nucleotides at 5' side of the cleavage site and a variable number to the 3' side of the cleavage site.

Only 3 known member of this class. Found in three plant pathogen (satellite RNAs of the tobacco ringspot virus,

required.

arabis mosaic virus and chicory yellow mottle virus) which uses RNA as the infectious agent (Figure 3).

Hepatitis Delta Virus (HDV) Ribozyme

Size: 50-60 nucleotides (at present)

5 Sequence requirements not fully determined.

Binding sites and structural requirements not fully determined, although no sequences 5' of cleavage site are

Only 1 known member of this class. Found in human HDV 10 (Figure 4).

Neurospora VS RNA Ribozyme

Size: ~144 nucleotides (at present)

Cleavage of target RNAs recently demonstrated.

Sequence requirements not fully determined.

15 Binding sites and structural requirements not fully determined. Only 1 known member of this class. Found in Neurospora VS RNA (Figure 5).

Table II: Human flt1 VEGF Receptor-Hammerhead Ribozyme and Substrate Sequence

20	nt.		HH Ri	Substrate				
	Posi- tion							
	10	GCCGAGAG	CUGAUGA	x	GAA	AGUGUCCG	CGGACACUC	CUCUCGGC
	13	GGAGCCGA	CUGAUGA	x	GAA	AGGAGUGU	ACACUCCUC	UCGGCUCC
25	15	GAGGAGCC	CUGAUGA	х	GAA	AGAGGAGU	ACUCCUCUC	GGCUCCUC
	20	CCGGGGAG	CUGAUGA	х	GAA	AGCCGAGA	UCUCGGCUC	CUCCCCGG
	23	CUGCCGGG	CUGAUGA	X	GAA	AGGAGCCG	CGGCUCCUC	CCCGGCAG
	43	CCCGCUCC	CUGAUGA	х	GAA	AGCCGCCG	CGGCGGCUC	GGAGCGGG
	54	GAGCCCCG	CUGAUGA	x	GAA	AGCCCGCU	AGCGGGCUC	CGGGGCUC
30	62	CUGCACCC	CUGAUGA	X	GAA	AGCCCCGG	CCGGGGCUC	GGGUGCAG
	97	CCCCGGGU	CUGAUGA	х	GAA	AUCCUCGC	GCGAGGAUU	ACCCGGGG
	98	UCCCCGGG	CUGAUGA	Х	GAA	AAUCCUCG	CGAGGAUUA	CCCGGGGA

	113	CAGGAGA	C CUGAUGA	A >	(GA)	A ACCACUUC	GAAGUGGU	U GUCUC <mark>CU</mark>
	116	AGCCAGG	A CUGAUGA	A >	(GA	A ACAACCAC	GUGGUUGU	UCCUGGC
	118	CCAGCCAG	G CUGAUGA	A X	GA/	A AGACAACC	GGUUGUCU	CUGGCUGG
	145	CGCGCCCI	J CUGAUGA	Х	GA/	A AGCGCCCG	CGGGCGCU	C AGGGCGC
5	185	GGCCGCC	A CUGAUGA	X	GAZ	AGUCCGUC	GACGGACU	UGGCGGC
	198	CGGCCAA	CUGAUGA	X	GAA	ACCCGGCC	GGCCGGGU	GUUGGCC
	201	CCCCGGCC	CUGAUGA	X	GAA	ACGACCCG	CGGGUCGU	J GGCCGGG
	240	GUGAGCG	CUGAUGA	X	GAA	ACGCGGCC	GGCCGCGU	GCGCUCAC
	246	ACCAUGGU	J CUGAUGA	X	GAA	AGCGCGAC	GUCGCGCUC	ACCAUGGU
10	25 5	CAGUAGCU	CUGAUGA	X	GAA	ACCAUGGU	ACCAUGGUC	AGCUACUG
	260	UGUCCCAG	CUGAUGA	X	GAA	AGCUGACC	GGUCAGCUA	CUGGGACA
	276	CACAGCAG	CUGAUGA	X	GAA	ACCCCGGU	ACCGGGGUC	CUGCUGUG
	294	AGACAGCU	CUGAUGA	Х	GAA	AGCAGCGC	GCGCUGCUC	AGCUG UC U
	301	GAGAAGCA	CUGAUGA	X	GAA	ACAGCUGA	UCAGCUGUC	ugcuucuc
15	306	CCUGUGAG	CUGAUGA	X	GAA	AGCAGACA	UGUCUGCUU	CUCACAGG
	307	UCCUGUGA	CUGAUGA	x	GAA	AAGCAGAC	GUCUGCUUC	UCACAGGA
*	309	GAUCCUGU	CUGAUGA	X	GAA	AGAAGCAG	CUGCUUCUC	ACAGGAUC
	317	CUGAACUA	CUGAUGA	Х	GAA	AUCCUGUG	CACAGGAUC	UAGUUCAG
	319	ACCUGAAC	CUGAUGA	X	GAA	AGAUCCUG	CAGGAUCUA	GUUCAGGU
20	322	UGAACCUG	CUGAUGA	Х	GAA	ACUAGAUC	GAUCUAGUU	CAGGUUCA
	323	UUGAACCU	CUGAUGA	X	GAA	AACUAGAU	AUCUAGUUC	AGGUUCAA
	328	UAAUUUUG	CUGAUGA	x	GAA	ACCUGAAC	GUUCAGGUU	CAAAAUUA
	32 9	UUUUAAUUU	CUGAUGA	Х	GAA	AACCUGAA	UUCAGGUUC	AAAAUUAA
	335	GAUCUUUU	CUGAUGA	Х	GAA	AUUUUGAA	UUCAAAAUU	AAAAGAUC
25	336	GGAUCUUU	CUGAUGA	Х	GAA	AAUUUUGA	UCAAAAUUA	AAAGAUCC
	343	CAGUUCAG	CUGAUGA	Х	GAA	AUCUUUUA	UAAAAGAUC	CUGAACUG
	355	GCCUUUUA	CUGAUGA	Х	GAA	ACUCAGUU	AACUGAGUU	UAAAAGGC
	356	UGCCUUUU	CUGAUGA	Х	GAA	AACUCAGU	ACUGAGUUU	AAAAGGCA
	357	GUGCCUUU	CUGAUGA	X	GAA	AAACUCAG	CUGAGUUUA	AAAGGCAC
30	375	GCUUGCAU	CUGAUGA	Х	GAA	AUGUGCUG	CAGCACAUC	AUGCAAGC
	400					AUGCAGUG		UCCAAUGC
	402		•			AGAUGCAG		CAAUGCAG
	427	AGACCAUU	CUGAUGA	X	GAA	AUGGGCUG	CAGCCCAUA	AAUGGUCU

	434	CAGGCAAA	CUGAUGA	X	GAA	ACCAUUUA	UAAAUGGUC	UUUGCCUG
	436	UUCAGGCA	CUGAUGA	X	GAA	AGACCAUU	AAUGGUCUU	UGCCUGAA
	437	UUUCAGGC	CUGAUGA	x	GAA	AAGACCAU	AUGGUCUUU	GCCUGAAA
	454	GCUUUCCU	CUGAUGA	x	GAA	ACUCACCA	UGGUGAGUA	AGGAAAGC
5	477	GAUUUAGU	CUGAUGA	x	GAA	AUGCUCAG	CUGAGCAUA	ACUAAAUC
	481	GGCAGAUU	CUGAUGA	X	GAA	AGUUAUGC	GCAUAACUA	AAUCUGCC
	485	CACAGGCA	CUGAUGA	X	GAA	AUUUAGUU	AACUAAAUC	UGCCUGUG
	51 2	UACUGCAG	CUGAUGA	x	GAA	AUUGUUUG	CAAACAAUU	CUGCAGUA
	51 3	GUACUGCA	CUGAUGA	x	GAA	AAUUGUUU	AAACAAUUC	UGCAGUAC
10	520	GGUUAAAG	CUGAUGA	х	GAA	ACUGCAGA	UCUGCAGUA	CUUUAACC
	52 3	CAAGGUUA	CUGAUGA	x	GAA	AGUACUGC	GCAGUACUU	UAACCUUG
	524	UCAAGGUU	CUGAUGA	Х	GAA	AAGUACUG	CAGUACUUU	AACCUUGA
	52 5	UUCAAGGU	CUGAUGA	Х	GAA	AAAGUACU	AGUACUUUA	ACCUUGAA
	530	CUGUGUUC	CUGAUGA	х	GAA	AGGUU AA A	UUUAACCUU	GAACACAG
15	541	GUUUGCUU	CUGAUGA	x	GAA	AGCUGUGU	ACACAGCUC	AAGCAAAC
	56 0	AGCUGUAG	CUGAUGA	x	GAA	AGCCAGUG	CACUGGCUU	CUACAGCU
	561	CAGCUGUA	CUGAUGA	X	GAA	AAGCCAGU	ACUGGCUUC	UACAGCUG
	56 3	UGCAGCUG	CUGAUGA	x	GAA	AGAAGCCA	UGGCUUCUA	CAGCUGCA
	575	CAGCUAGA	CUGAUGA	x	GAA	AUUUGCAG	CUGCAAAUA	UCUAGCUG
20	5 7 7	UACAGCUA	CUGAUGA	х	GAA	AUAUUUGC	GCAAAUAUC	UAGCUGUA
	579	GGUACAGC	CUGAUGA	x	GAA	AGAUAUUU	AAAUAUCUA	GCUGUACO
	58 5	GAAGUAGG	CUGAUGA	х	GAA	ACAGCUAG	CUAGCUGUA	CCUACUUC
	58 9	CUUUGAAG.	CUGAUGA	х	GAA	AGGUACAG	CUGUACCUA	CUUCAAAG
	592	CUUCUUUG	CUGAUGA	Х	GAA	AGUAGGUA	UACCUACUU	CAAAGAAG
25	593	טכטטכטטט	CUGAUGA	X	GAA	AAGUAGGU	ACCUACUUC	AAAGAAGA
	614	AGAUUGCA	CUGAUGA	Х	GAA	AUUCUGUU	AACAGAAUC	UGCAAUCU
	621	AAUAUAUA	CUGAUGA	X	GAA	AUUGCAGA	UCUGCAAUC	UAUAUAUU
	623	AUAUAAAU	CUGAUGA	X	GAA	AGAUUGCA	UGCAAUCUA	AUUUAUAU
	625	AAUAAAUA'	CUGAUGA	X	GAA	AUAGAUUG	CAAUCUAUA	UAUUUAUU
30	627	CUAAUAAA	CUGAUGA	x	GAA	AUAUAGAU	AUCUAUAUA	UUUAUUAG
	629	CACUAAUA	CUGAUGA	х	GAA	AUAUAUAG	CUAUAUAUU	UAUUAGUG
	630	UCACUAAU	CUGAUGA	X	GAA	AAUAUAUA	UUUAUAUUU	AUUAGUGA
	631	AUCACUAA	CUGAUGA	Х	GAA	AAAUAUAU	AUAUAUUUA	UUAGUGAU

	633	GUAUCACU CUGAUGA X GAA AUAAAUAU	AUAUUUAUU AGUGAUAC
	634	UGUAUCAC CUGAUGA X GAA AAUAAAUA	UAUUUAUUA GUGAUACA
	64 0	UCUACCUG CUGAUGA X GAA AUCACUAA	UUAGUGAUA CAGGUAGA
	64 6	GAAAGGUC CUGAUGA X GAA ACCUGUAU	AUACAGGUA GACCUUUC
5	652	CUCUACGA CUGAUGA X GAA AGGUCUAC	GUAGACCUU UCGUAGAG
	653	UCUCUACG CUGAUGA X GAA AAGGUCUA	UAGACCUUU CGUAGAGA
	654	AUCUCUAC CUGAUGA X GAA AAAGGUCU	AGACCUUUC GUAGAGAU
	657	UACAUCUC CUGAUGA X GAA ACGAAAGG	CCUUUCGUA GAGAUGUA
	665	UUUCACUG CUGAUGA X GAA ACAUCUCU	AGAGAUGUA CAGUGAAA
10	67 5	AUUUCGGG CUGAUGA X GAA AUUUCAÇU	AGUGAAAUC CCCGAAAU
	684	AUGUGUAU CUGAUGA X GAA AUUUCGGG	CCCGAAAUU AUACACAU
	685	CAUGUGUA CUGAUGA X GAA AAUUUCGG	CCGAAAUUA UACACAUG
	687	GUCAUGUG CUGAUGA X GAA AUAAUUUC	GAAAUUAUA CACAUGAC
	711	GGAAUGAC CUGAUGA X GAA AGCUCCCU	AGGGAGCUC GUCAUUCC
15	714	CAGGGAAU CUGAUGA X GAA ACGAGCUC	GAGCUCGUC AUUCCCUG
	717	CGGCAGGG CUGAUGA X GAA AUGACGAG	CUCGUCAUU CCCUGCCG
	718	CCGGCAGG CUGAUGA X GAA AAUGACGA	UCGUCAUUC CCUGCCGG
	729	GGUGACGU CUGAUGA X GAA ACCCGGCA	UGCCGGGUU ACGUCACC
	730	AGGUGACG CUGAUGA X GAA AACCCGGC	GCCGGGUUA CGUCACCU
20	734	UGUUAGGU CUGAUGA X GAA ACGUAACC	GGUUACGUC ACCUAACA
	739	AGUGAUGU CUGAUGA X GAA AGGUGACG	CGUCACCUA ACAUCACU
	744	GUAACAGU CUGAUGA X GAA AUGUUAGG	CCUAACAUC ACUGUUAC
	750	UUUAAAGU CUGAUGA X GAA ACAGUGAU	AUCACUGUU ACUUUAAA
	751	UUUUAAAG CUGAUGA X GAA AACAGUGA	UCACUGUUA CUUUAAAA
25	754	CUUUUUUA CUGAUGA X GAA AGUAACAG	CUGUUACUU UAAAAAAG
	755	ACUUUUUU CUGAUGA X GAA AAGUAACA	UGUUACUUU AAAAAAGU
	756	AACUUUUU CUGAUGA X GAA AAAGUAAC	GUUACUUUA AAAAAGUU
	764	CAAGUGGA CUGAUGA X GAA ACUUUUUU	AAAAAAGUU UCCACUUG
	765	UCAAGUGG CUGAUGA X GAA AACUUUUU	AAAAAGUUU CCACUUGA
30	766	GUCAAGUG CUGAUGA X GAA AAACUUUU	AAAAGUUUC CACUUGAC
	771	AAAGUGUC CUGAUGA X GAA AGUGGAAA	UUUCCACUU GACACUUU
	778	AGGGAUCA CUGAUGA X GAA AGUGUCAA	UUGACACUU UGAUCCCU
	779	CAGGGAUC CUGAUGA X GAA AAGUGUCA	UGACACUUU GAUCCCUG

	783	CCAUCAGG	CUGAUGA	Х	GAA	AUCAAAGU	ACUUUGAUC	CCUGAUGG
	801	UCCCAGAU	CUGAUGA	Х	GAA	AUGCGUUU	AAACGCAUA	AUCUGGGA
	804	CUGUCCCA	CUGAUGA	Х	GAA	AUUAUGCG	CGCAUAAUC	UGGGACAG
	814	GCCCUUUC	CUGAUGA	Х	GAA	ACUGUCCC	GGGACAGUA	GAAAGGGC
5	824	AUAUGAUG	CUGAUGA	X	GAA	AGCCCUUU	AAAGGGCUU	CAUCAUAU
	825	GAUAUGAU	CUGAUGA	Х	GAA	AAGCCCUU	AAGGGCUUC	AUCAUAUC
	828	UUUGAUAU	CUGAUGA	Х	GAA	AUGAAGCC	GGCUUCAUC	AUAUCAAA
	831	GCAUUUGA	CUGAUGA	X	GAA	AUGAUGAA	UUCAUCAUA	UCAAAUGC
,	833	UUGCAUUU	CUGAUGA	X	GAA	AUAUGAUG	CAUCAUAUC	AAAUGCAA
10	845	UUUCUUUG	CUGAUGA	X	GAA	ACGUUGCA	UGCAACGUA	CAAAGAAA
	85 5	AGAAGCCC	CUGAUGA	Х	GAA	AUUUCUUU	AAAGAAAUA	GGGCUUCU
	861	CAGGUCAG	CUGAUGA	Х	GAA	AGCCCUAU	AUAGGGCUU	CUGACCUG
	862	ACAGGUCA	CUGAUGA	Х	GAA	AAGCCCUA	UAGGCUUC	UGACCUGU
	882	UGCCCAUU	CUGAUGA	X	GAA	ACUGUUGC	GCAACAGUC	AAUGGGCA
15	892	CUUAUACA	CUGAUGA	X	GAA	AUGCCCAU	AUGGGCAUU	UGUAUAAG
	893	UCUUAUAC	CUGAUGA	Х	GAA	AAUGCCCA	UGGGCAUUU	GUAUAAGA
	896	UUGUCUUA	CUGAUGA	X	GAA	ACAAAUGC	GCAUUUGUA	UAAGACAA
	898	GUUUGUCU	CUGAUGA	Х	GAA	AUACAAAU	AUUUGUAUA	AGACAAAC
	908	GUGUGAGA	CUGAUGA	X	GAA	AGUUUGUC	GACAAACUA	UCUCACAC
20	910	AUGUGUGA	CUGAUGA	X	GAA	AUAGUUUG	CAAACUAUC	UCACACAU
	912	CGAUGUGU	CUGAUGA	Х	GAA	AGAUAGUU	AACUAUCUC	ACACAUCG
	919	GGUUUGUC	CUGAUGA	Х	GAA	AUGUGUGA	UCACACAUC	GACAAACC
	931	UAUGAUUG	CUGAUGA	X	GAA	AUUGGUUU	AAACCAAUA	CAAUCAUA
	936	ACAUCUAU	CUGAUGA	X	GAA	AUUGUAUU	AAUACAAUC	AUAGAUGU
25	939	UGGACAUC	CUGAUGA	X	GAA	AUGAUUGU	ACAAUCAUA	GAUGUCCA
	945	CUUAUUUG	CUGAUGA	X	GAA	ACAUCUAU	AUAGAUGUC	CAAAUAAG
	951	GGUGUGCU	CUGAUGA	X	GAA	AUUUGGAC	GUCCAAAUA	AGCACACC
	969	AGUAAUUU	CUGAUGA	X	GAA	ACUGGGCG	CGCCCAGUC	AAAUUACU
	974	CUCUAAGU	CUGAUGA	X	GAA	AUUUGACU	AGUCAAAUU	ACUUAGAG
30	975	CCUCUAAG	CUGAUGA	X	GAA	AAUUUGAC	GUCAAAUUA	CUUAGAGG
	978	UGGCCUCU	CUGAUGA	X	GAA	AGUAAUUU	AAAUUACUU	AGAGGCCA
	97 9	AUGGCCUC	CUGAUGA	X	GAA	AAGUAAUU	AAUUACUUA	GAGGCCAU
	988	GACAAGAG	CUGAUGA	. X	GAA	AUGGCCUC	GAGGCCAUA	cucuuguc

	991	GAGGACAA CUGAUGA X GAA AGUAUGGC	GCCAUACUC UUGUCCUC
	993	UUGAGGAC CUGAUGA X GAA AGAGUAUG	CAUACUCUU GUCCUCAA
	996	CAAUUGAG CUGAUGA X GAA ACAAGAGU	ACUCUUGUC CUCAAUUG
	999	GUACAAUU CUGAUGA X GAA AGGACAAG	CUUGUCCUC AAUUGUAC
5	1003	B AGCAGUAC CUGAUGA X GAA AUUGAGGA	UCCUCAAUU GUACUGCU
	1006	GGUAGCAG CUGAUGA X GAA ACAAUUGA	UCAAUUGUA CUGCUACC
	1012	GGGAGUGG CUGAUGA X GAA AGCAGUAC	GUACUGCUA CCACUCCC
	1018	GUUCAAGG CUGAUGA X GAA AGUGGUAG	CUACCACUC CCUUGAAC
	1022	UCGUGUUC CUGAUGA X GAA AGGGAGUG	CACUCCCUU GAACACGA
10	1035	GUCAUUUG CUGAUGA X GAA ACUCUCGU	ACGAGAGUU CAAAUGAC
	1036	GGUCAUUU CUGAUGA X GAA AACUCUCG	CGAGAGUUC AAAUGACC
	1051	AUCAGGGU CUGAUGA X GAA ACUCCAGG	CCUGGAGUU ACCCUGAU
	1052	CAUCAGGG CUGAUGA X GAA AACUCCAG	CUGGAGUUA CCCUGAUG
	1069	AGCUCUCU CUGAUGA X GAA AUUUUUUU	AAAAAAAUA AGAGAGCU
15	1078	CCUUACGG CUGAUGA X GAA AGCUCUCU	AGAGAGCUU CCGUAAGG
	1079	GCCUUACG CUGAUGA X GAA AAGCUCUC	GAGAGCUUC CGUAAGGC
	1083	CGUCGCCU CUGAUGA X GAA ACGGAAGC	GCUUCCGUA AGGCGACG
	1095	CUUUGGUC CUGAUGA X GAA AUUCGUCG	CGACGAAUU GACCAAAG
	1108	GGCAUGGG CUGAUGA X GAA AUUGCUUU	AAAGCAAUU CCCAUGCC
20	1109	UGGCAUGG CUGAUGA X GAA AAUUGCUU	AAGCAAUUC CCAUGCCA
	1122	CUGUAGAA CUGAUGA X GAA AUGUUGGC	GCCAACAUA UUCUACAG
	1124	CACUGUAG CUGAUGA X GAA AUAUGUUG	CAACAUAUU CUACAGUG
	1125	ACACUGUA CUGAUGA X GAA AAUAUGUU	AACAUAUUC UACAGUGU
	1127	GAACACUG CUGAUGA X GAA AGAAUAUG	CAUAUUCUA CAGUGUUC
25	1134	AUAGUAAG CUGAUGA X GAA ACACUGUA	UACAGUGUU CUUACUAU
	1135	AAUAGUAA CUGAUGA X GAA AACACUGU	ACAGUGUUC UUACUAUU
	1137	UCAAUAGU CUGAUGA X GAA AGAACACU	AGUGUUCUU ACUAUUGA
	1138	GUCAAUAG CUGAUGA X GAA AAGAACAC	GUGUUCUUA CUAUUGAC
	1141	UUUGUCAA CUGAUGA X GAA AGUAAGAA	UUCUUACUA UUGACAAA
0	1143	AUUUUGUC CUGAUGA X GAA AUAGUAAG	CUUACUAUU GACAAAAU
	1173	CAAGUAUA CUGAUGA X GAA AGUCCUUU	AAAGGACUU UAUACUUG
	1174	ACAAGUAU CUGAUGA X GAA AAGUCCUU	AAGGACUUU AUACUUGU
	1175	GACAAGUA CUGAUGA X GAA AAAGUCCU	AGGACUUUA UACUUGUC

	1177	ACGACAAG	CUGAUGA	X	GAA	AUAAAGUC	GACUUUAUA	CUUGUCGU
	1180	UACACGAC	CUGAUGA	х	GAA	AGUAUAAA	UUUAUACUU	GUCGUGUA
	1183	CCUUACAC	CUGAUGA	X	GAA	ACAAGUAU	AUACUUGUC	GUGUAAGG
	1188	CCACUCCU	CUGAUGA	Х	GAA	ACACGACA	UGUCGUGUA	AGGAGUGG
5	1202	AUUUGAAU	CUGAUGA	Х	GAA	AUGGUCCA	UGGACCAUC	AUUCAAAU
	1205	CAGAUUUG	CUGAUGA	Х	GAA	AUGAUGGU	ACCAUCAUU	CAAAUCUG
	1206	ACAGAUUU	CUGAUGA	Х	GAA	AAUGAUGG	CCAUCAUUC	AAAUCUGU
	1211	UGUUAACA	CUGAUGA	Х	ĠAA	AUUUGAAU	AUUCAAAUC	UGUUAACA
	1215	GAGGUGUU	CUGAUGA	Х	GAA	ACAGAUUU	AAAUCUGUU	AACACCUC
10	1216	UGAGGUGU	CUGAUGA	Х	GAA	AACAGAUU	AAUCUGUUA	ACACCUCA
	1223	UAUGCACU	CUGAUGA	Х	GAA	AGGUGUUA	UAACACCUC	AGUGCAUA
	1231	AUCAUAUA	CUGAUGA	х	GAA	AUGCACUG	CAGUGCAUA	UAUAUGAU
	1233	UUAUCAUA	CUGAUGA	X	GAA	AUAUGCAC	GUGCAUAUA	UAUGAUAA
	1235	CUUUAUCA	CUGAUGA	X	GAA	AUAUAUGC	GCAUAUAUA	UGAUAAAG
15	1240	GAAUGCUU	CUGAUGA	X	GAA	AUCAUAUA	UAUAUGAUA	AAGCAUUC
	1247	CAGUGAUG	CUGAUGA	Х	GAA	AUGCUUUA	UAAAGCAUU	CAUCACUG
	1248	ACAGUGAU	CUGAUGA	Х	GAA	AAUGCUUU	AAAGCAUUC	AUCACUGU
	1251	UUCACAGU	CUGAUGA	Х	GAA	AUGAAUGC	GCAUUCAUC	ACUGUGAA
	1264	CUGUUUUC	CUGAUGA	X	GAA	AUGUUUCA	UGAAACAUC	GAAAACAG
20	1281	ACGGUUUC	CUGAUGA	Х	GAA	AGCACCUG	CAGGUGCUU	GAAACCGU
	1290	UUGCCAGC	CUGAUGA	X	GAA	ACGGUUUC	GAAACCGUA	GCUGGCAA
	1304	GCCGGUAA	CUGAUGA	Х	GAA	ACCGCUUG	CAAGCGGUC	UUACCGGC
	1306	GAGCCGGU	CUGAUGA	X	GAA	AGACCGCU	AGCGGUCUU	ACCGGCUC
	1307	AGAGCCGG	CUGAUGA	X	GAA	AAGACCGC	GCGGUCUUA	CCGGCUCU
25	1314	UUCAUAGA	CUGAUGA	X	GAA	AGCCGGUA	UACCGGCUC	UCUAUGAA
	1316	CUUUCAUA	CUGAUGA	X	GAA	AGAGCCGG	CCGGCUCUC	UAUGAAAG
	1318	CACUUUCA	CUGAUGA	X	GAA	AGAGAGCC	GGCUCUCUA	UGAAAGUG
	1334	GCGAGGGA	CUGAUGA	X	GAA	AUGCCUUC	GAAGGCAUU	UCCCUCGC
	1335	GGCGAGGG	CUGAUGA	X	GAA	AAUGCCUU	AAGGCAUUU	CCCUCGCC
30	1336	CGGCGAGG	CUGAUGA	Х	GAA	AAAUGCCU	AGGCAUUUC	CCUCGCCG
	1340	CUUCCGGC	CUGAUGA	X	GAA	AGGGAAAU	AUUUCCCUC	GCCGGAAG
	1350	AACCAUAC	CUGAUGA	X	GAA	ACUUCCGG	CCGGAAGUU	GUAUGGUU
	1353	UUUAACCA	CUGAUGA	Х	GAA	ACAACUUC	GAAGUUGUA	UGGUUAAA

÷

	1358	CAUCUUUU CUGAUGA X GAA ACCAUAC	A UGUAUGGUU AAAAGAUG
	1359	CCAUCUUU CUGAUGA X GAA AACCAUA	C GUAUGGUUA AAAGAUGG
	1370	UCGCAGGU CUGAUGA X GAA ACCCAUC	U AGAUGGGUU ACCUGCGA
	1371	. GUCGCAGG CUGAUGA X GAA AACCCAU	C GAUGGGUUA CCUGCGAC
5	1388	AGCGAGCA CUGAUGA X GAA AUUUCUC	A UGAGAAAUC UGCUCGCU
	1393	CAAAUAGC CUGAUGA X GAA AGCAGAU	U AAUCUGCUC GCUAUUUG
	1397	GAGUCAAA CUGAUGA X GAA AGCGAGCA	A UGCUCGCUA UUUGACUC
	1399	ACGAGUCA CUGAUGA X GAA AUAGCGAG	G CUCGCUAUU UGACUCGU
	1400	CACGAGUC CUGAUGA X GAA AAUAGCGA	UCGCUAUUU GACUCGUG
10	1405	GUAGCCAC CUGAUGA X GAA AGUCAAAI	J AUUUGACUC GUGGCUAC
	1412	UUAACGAG CUGAUGA X GAA AGCCACGA	UCGUGGCUA CUCGUUAA
	1415	UAAUUAAC CUGAUGA X GAA AGUAGCCA	UGGCUACUC GUUAAUUA
	1418	UGAUAAUU CUGAUGA X GAA ACGAGUAG	CUACUCGUU AAUUAUCA
	1419	UUGAUAAU CUGAUGA X GAA AACGAGUA	UACUCGUUA AUUAUCAA
15	1422	UCCUUGAU CUGAUGA X GAA AUUAACGA	UCGUUAAUU AUCAAGGA
	1423	GUCCUUGA CUGAUGA X GAA AAUUAACG	CGUUAAUUA UCAAGGAC
	1425	ACGUCCUU CUGAUGA X GAA AUAAUUAA	UUAAUUAUC AAGGACGU
	1434	UCUUCAGU CUGAUGA X GAA ACGUCCUU	AAGGACGUA ACUGAAGA
	1456	GAUUGUAU CUGAUGA X GAA AUUCCCUG	CAGGGAAUU AUACAAUC
20	1457	AGAUUGUA CUGAUGA X GAA AAUUCCCU	AGGGAAUUA UACAAUCU
	1459	CAAGAUUG CUGAUGA X GAA AUAAUUCC	GGAAUUAUA CAAUCUUG
	1464	CUCAGCAA CUGAUGA X GAA AUUGUAUA	UAUACAAUC UUGCUGAG
	1466	UGCUCAGC CUGAUGA X GAA AGAUUGUA	UACAAUCUU GCUGAGCA
	1476	GACUGUUU CUGAUGA X GAA AUGCUCAG	CUGAGCAUA AAACAGUC
25	1484	ACACAUUU CUGAUGA X GAA ACUGUUUU	AAAACAGUC AAAUGUGU
	1493	GGUUUUUA CUGAUGA X GAA ACACAUUU	AAAUGUGUU UAAAAACC
	1494	AGGUUUUU CUGAUGA X GAA AACACAUU	AAUGUGUUU AAAAACCU
	1495	GAGGUUUU CUGAUGA X GAA AAACACAU	AUGUGUUUA AAAACCUC
	1503	GUGGCAGU CUGAUGA X GAA AGGUUUUU	AAAAACCUC ACUGCCAC
30	1513	GACAAUUA CUGAUGA X GAA AGUGGCAG	CUGCCACUC UAAUUGUC
	1515	UUGACAAU CUGAUGA X GAA AGAGUGGC	GCCACUCUA AUUGUCAA
	1518	ACAUUGAC CUGAUGA X GAA AUUAGAGU	ACUCUAAUU GUCAAUGU
	1521	UUCACAUU CUGAUGA X GAA ACAAUUAG	CUAAUUGUC AAUGUGAA

	1539	UUUUCGUA	CUGAUGA	X	GAA	AUCUGGGG	CCCCAGAUU	UACGAAAA
	1540	CUUUUCGU	CUGAUGA	X	GAA	AAUCUGGG	CCCAGAUUU	ACGAAAAG
	1541	CCUUUUCG	CUGAUGA	X	GAA	AAAUCUGG	CCAGAUUUA	CGAAAAGG
	1556	GAAACGAU	CUGAUGA	X	GAA	ACACGGCC	GGCCGUGUC	AUCGUUUC
5	1559	CUGGAAAC	CUGAUGA	X	GAA	AUGACACG	CGUGUCAUC	GUUUCCAG
	1562	GGUCUGGA	CUGAUGA	X	GAA	ACGAUGAC	GUCAUCGUU	UCCAGACC
	1563	GGGUCUGG	CUGAUGA	Х	GAA	AACGAUGA	UCAUCGUUU	CCAGACCC
	1564	CGGGUCUG	CUGAUGA	X	GAA	AAACGAUG	CAUCGUUUC	CAGACCCG
	1576	UGGGUAGA	CUGAUGA	Х	GAA	AGCCGGGU	ACCCGGCUC	UCUACCCA
10	1578	AGUGGGUA	CUGAUGA	Х	GAA	AGAGCCGG	CCGGCUCUC	UACCCACU
	1580	CCAGUGGG	CUGAUGA	Х	GAA	AGAGAGCC	GGCUCUCUA	CCCACUGG
	1602	CAAGUCAG	CUGAUGA	X	GAA	AUUUGUCU	AGACAAAUC	CUGACUUG
	1609	UGCGGUAC	CUGAUGA	X	GAA	AGUCAGGA	UCCUGACUU	GUACCGCA
	1612	AUAUGCGG	CUGAUGA	Х	GAA	ACAAGUCA	UGACUUGUA	CCGCAUAU
15	1619	GGAUACCA	CUGAUGA	Х	GAA	AUGCGGUA	UACCGCAUA	UGGUAUCC
	1624	UUGAGGGA	CUGAUGA	Х	GAA	ACCAUAUG	CAUAUGGUA	UCCCUCAA
	1626	GGUUGAGG	CUGAUGA	Х	GAA	AUACCAUA	UAUGGUAUC	CCUCAACC
	1630	UGUAGGUU	CUGAUGA	X	GAA	AGGGAUAC	GUAUCCCUC	AACCUACA
	1636	CUUGAUUG	CUGAUGA	X	GAA	AGGUUGAG	CUCAACCUA	CAAUCAAG
20	1641	AACCACUU	CUGAUGA	X	GAA	AUUGUAGG	CCUACAAUC	AAGUGGUU
	1649	GGUGCCAG	CUGAUGA	X	GAA	ACCACUUG	CAAGUGGUU	CUGGCACC
	1650	GGGUGCCA	CUGAUGA	X	GAA	AACCACUU	AAGUGGUUC	UGGCACCC
	1663	AUUAUGGU	CUGAUGA	X	GAA	ACAGGGGU	ACCCCUGUA	ACCAUAAU
	1669	GGAAUGAU	CUGAUGA	X	GAA	AUGGUUAC	GUAACCAUA	AUCAUUCC
25	1672	UUCGGAAU	CUGAUGA	X	GAA	AUUAUGGU	ACCAUAAUC	AUUCCGAA
	1675	UGCUUCGG	CUGAUGA	X	GAA	AUGAUUAU	AUAAUCAUU	CCGAAGCA
	1676	UUGCUUCG	CUGAUGA	X	GAA	AAUGAUUA	UAAUCAUUC	CGAAGCAA
	1694	UGGAACAA	CUGAUGA	X	GAA	AGUCACAC	GUGUGACUU	UUGUUCCA
	1695	UUGGAACA	CUGAUGA	X	GAA	AAGUCACA	UGUGACUUU	UGUUCCAA
30	1696	AUUGGAAC	CUGAUGA	X	GAA	AAAGUCAC	GUGACUUUU	GUUCCAAU
	1699	AUUAUUGG	CUGAUGA	X	GAA	ACAAAAGU	ACUUUUGUU	CCAAUAAU
	1700	CAUUAUUG	CUGAUGA	X	GAA	AACAAAAG	CUUUUGUUC	CAAUAAUG
	1705	CUCUUCAU	CUGAUGA	Х	GAA	AUUGGAAC	GUUCCAAUA	AUGAAGAG

	1715	GGAUAAAG	CUGAUGA	2	(GA	ACUCUUCA	UGAAGAGUC	CUUUAUCC
	1718	CCAGGAUA	CUGAUGA	×	GA,	AGGACUCU	AGAGUCCUU	UAUCCUGG
	1719	UCCAGGAU	CUGAUGA	X	GAA	AAGGACUC	GAGUCCUUU	AUCCUGGA
	1720	AUCCAGGA	CUGAUGA	X	GAA	AAAGGACU	AGUCCUUUA	UCCUGGAU
5	1722	GCAUCCAG	CUGAUGA	X	GAA	AUAAAGGA	UCCUUUAUC	CUGGAUGC
	1755	AUGCUCUC	CUGAUGA	X	GAA	AUUCUGUU	AACAGAAUU	GAGAGCAU
	1764	CGCUGAGU	CUGAUGA	Х	GAA	AUGCUCUC	GAGAGCAUC	ACUCAGCG
	1768	CAUGCGCU	CUGAUGA	X	GAA	AGUGAUGC	GCAUCACUC	AGCGCAUG
	1782	CCUUCUAU	CUGAUGA	Х	GAA	AUUGCCAU	AUGGCAAUA	AUAGAAGG
10	1785	UUUCCUUC	CUGAUGA	Х	GAA	AUUAUUGC	GCAAUAAUA	GAAGGAAA
	1798	AGCCAUCU	CUGAUGA	Х	GAA	AUUCUUUC	GAAAGAAUA	AGAUGGCU
	1807	CAAGGUGC	CUGAUGA	Х	GAA	AGCCAUCU	AGAUGGCUA	GCACCUUG
	1814	CCACAACC	CUGAUGA	Х	GAA	AGGUGCUA	UAGCACCUU	GGUUGUGG
	1818	UCAGCCAC	CUGAUGA	Х	GAA	ACCAAGGU	ACCUUGGUU	GUGGCUGA
15	1829	AAAUUCUA	CUGAUGA	X	GAA	AGUCAGCC	GGCUGACUC	UAGAAUUU
	1831	AGAAAUUC	CUGAUGA	Х	GAA	AGAGUCAG	CUGACUCUA	GAAUUUCU
	1836	AUUCCAGA	CUGAUGA	х	GAA	AUUCUAGA	UCUAGAAUU	UCUGGAAU
	1837	GAUUCCAG	CUGAUGA	X	GAA	AAUUCUAG	CUAGAAUUU	CUGGAAUC
	1838	AGAUUCCA	CUGAUGA	X	GAA	AAAUUCUA	UAGAAUUUC	UGGAAUCU
20	1845	CAAAUGUA	CUGAUGA	x	GAA	AUUCCAGA	UCUGGAAUC	UACAUUUG
	1847	UGCAAAUG	CUGAUGA	X	GAA	AGAUUCCA	UGGAAUCUA	CAUUUGCA
	1851	GCUAUGCA	CUGAUGA	X	GAA	AUGUAGAU	AUCUACAUU	UGCAUAGC
	1852	AGCUAUGC	CUGAUGA	x	GAA	AAUGUAGA	UCUACAUUU	GCAUAGCU
	1857	UUGGAAGC	CUGAUGA	X	GAA	AUGCAAAU	AUUUGCAUA	GCUUCCAA
25	1861	UUUAUUGG	CUGAUGA	X	GAA	AGCUAUGC	GCAUAGCUU	CCAAUAAA
	1862	CUUUAUUG	CUGAUGA	X	GAA	AAGCUAUG	CAUAGCUUC	CAAUAAAG
	1867	CCCAACUU	CUGAUGA	X	GAA	AUUGGAAG	CUUCCAAUA	AAGUUGGG
	1872	ACAGUCCC	CUGAUGA	X	GAA	ACUUUAUU	AAUAAAGUU	GGGACUGU
	1893	UAAAAGCU	CUGAUGA	Х	GAA	AUGUUUCU	AGAAACAUA	AGCUUUUA
30	1898	UGAUAUAA	CUGAUGA	X	GAA	AGCUUAUG	CAUAAGCUU	UUAUAUCA
	1899	GUGAUAUA	CUGAUGA	X	GAA	AAGCUUAU	AUAAGCUUU 1	UAUAUCAC
	1900	UGUGAUAU	CUGAUGA	X	GAA	AAAGCUUA	UAAGCUUUU 2	AUAUCACA
	1901	CUGUGAUA	CUGAUGA	X	GAA	AAAAGCUU	AAGCUUUUA I	UAUCACAG

	1903	AUCUGUGA	CUGAUGA	X	GAA	AUAAAAGC	GCUUUUAUA	UCACAGAU
	1905	ACAUCUGU	CUGAUGA	X	GAA	A AA AUAUA	UUUUAUAUC	ACAGAUGU
	1925	UAACAUGA	CUGAUGA	X	GAA	ACCCAUUU	AAAUGGGUU	UCAUGUUA
	1926	UUAACAUG	CUGAUGA	X	GAA	AACCCAUU	AAUGGGUUU	CAUGUUAA
5	1927	GUUAACAU	CUGAUGA	X	GAA	AAACCCAU	AUGGGUUUC	AUGUUAAC
	1932	UCCAAGUU	CUGAUGA	Х	GAA	ACAUGAAA	UUUCAUGUU	AACUUGGA
	1933	UUCCAAGU	CUGAUGA	Х	GAA	AACAUGAA	UUCAUGUUA	ACUUGGAA
	1937	υυυυυυςς	CUGAUGA	X	GAA	AGUUAACA	UGUUAACUU	GGAAAAA
	1976	CUGUGCAA	CUGAUGA	X	GAA	ACAGUUUC	GAAACUGUC	UUGCACAG
10	1978	AACUGUGC	CUGAUGA	Х	GAA	AGACAGUU	AACUGUCUU	GCACAGUU
	1986	AACUUGUU	CUGAUGA	Х	GAA	ACUGUGCA	UGCACAGUU	AACAAGUU
	1987	GAACUUGU	CUGAUGA	X	GAA	AACUGUGC	GCACAGUUA	ACAAGUUC
	1994	UGUAUAAG	CUGAUGA	Х	GAA	ACUUGUUA	UAACAAGUU	CUUAUACA
	1995	CUGUAUAA	CUGAUGA	X	GAA	AACUUGUU	AACAAGUUC	UUAUACAG
15	1997	CUCUGUAU	CUGAUGA	Х	GAA	AGAACUUG	CAAGUUCUU	AUACAGAG
	1998	UCUCUGUA	CUGAUGA	X	GAA	AAGAACUU	AAGUUCUUA	UACAGAGA
	2000	CGUCUCUG	CUGAUGA	Х	GAA	AUAAGAAC	GUUCUUAUA	CAGAGACG
	2010	AUCCAAGU	CUGAUGA	Х	GAA	ACGUCUCU	AGAGACGUU	ACUUGGAU
	2011	AAUCCAAG	CUGAUGA	Х	GAA	AACGUCUC	GAGACGUUA	CUUGGAUU
20	2014	UAAAAUCC	CUGAUGA	Х	GAA	AGUAACGU	ACGUUACUU	GGAUUUUA
	2019	CGCAGUAA	CUGAUGA	X	GAA	AUCCAAGU	ACUUGGAUU	UUACUGCG
	2020	CCGCAGUA	CUGAUGA	Х	GAA	AAUCCAAG	CUUGGAUUU	UACUGCGG
	2021	UCCGCAGU	CUGAUGA	х	GAA	AAAUCCAA	UUGGAUUUU	ACUGCGGA
	2022	GUCCGCAG	CUGAUGA	Х	GAA	AAAAUCCA	UGGAUUUUA	CUGCGGAC
25	2034	CUGUUAUU	CUGAUGA	Х	GAA	ACUGUCCG	CGGACAGUU	AAUAACAG
	2035	UCUGUUAU	CUGAUGA	Х	GAA	AACUGUCC	GGACAGUUA	AUAACAGA
	2038	UGUUCUGU	CUGAUGA	х	GAA	AUUAACUG	CAGUUAAUA	ACAGAACA
	2054	UAAUACUG	CUGAUGA	х	GAA	AGUGCAUU	AAUGCACUA	CAGUAUUA
	2059	CUUGCUAA	CUGAUGA	x	GAA	ACUGUAGU	ACUACAGUA	UUAGCAAG
30	2061	UGCUUGCU	CUGAUGA	X	GAA	AUACUGUA	UACAGUAUU	AGCAAGCA
	2062	UUGCUUGC	CUGAUGA	Х	GAA	AAUACUGU	ACAGUAUUA	GCAAGCAA
	2082	UCCUUAGU	CUGAUGA	X	GAA	AUGGCCAU	AUGGCCAUC	ACUAAGGA
	2086	GUGCUCCU	CUGAUGA	х	GAA	AGUGAUGG	CCAUCACUA	AGGAGCAC

	2096	GAGUGAUG	CUGAUGA	. }	GA/	A AGUGCUCC	GGAGCACUC CAUCACUC
	2100	UUAAGAGU	J CUGAUGA	. }	(GA	AUGGAGUG	CACUCCAUC ACUCUUAA
	2104	AAGAUUAA	CUGAUGA	. X	GA	AGUGAUGG	CCAUCACUC UUAAUCUU
	2106	GUAAGAUU	CUGAUGA	. X	GAA	AGAGUGAU	AUCACUCUU AAUCUUAC
5	2107	GGUAAGAU	CUGAUGA	. X	GAA	AAGAGUGA	UCACUCUUA AUCUUACC
	2110	GAUGGUAA	. CUGAUGA	Х	GAA	AUUAAGAG	CUCUUAAUC UUACCAUC
	2112	AUGAUGGU	CUGAUGA	Х	GAA	AGAUUAAG	CUUAAUCUU ACCAUCAU
	2113	CAUGAUGG	CUGAUGA	Х	GAA	AAGAUUAA	UUAAUCUUA CCAUCAUG
	2118	ACAUUCAU	CUGAUGA	X	GAA	AUGGUAAG	CUUACCAUC AUGAAUGU
10	2127	UGCAGGGA	CUGAUGA	Х	GAA	ACAUUCAU	AUGAAUGUU UCCCUGCA
	2128	UUGCAGGG	CUGAUGA	Х	GAA	AACAUUCA	UGAAUGUUU CCCUGCAA
	2129	CUUGCAGG	CUGAUGA	Х	GAA	AAACAUUC	GAAUGUUUC CCUGCAAG
	2140	GGUGCCUG	CUGAUGA	Х	GAA	AUCUUGCA	UGCAAGAUU CAGGCACC
	2141	AGGUGCCU	CUGAUGA	X	GAA	AAUCUUGC	GCAAGAUUC AGGCACCU
15	2150	UGCAGGCA	CUGAUGA	X	GAA	AGGUGCCU	AGGCACCUA UGCCUGCA
	2172	CCUGUGUA	CUGAUGA	X	GAA	ACAUUCCU	AGGAAUGUA UACACAGG
	2174	CCCCUGUG	CUGAUGA	X	GAA	AUACAUUC	GAAUGUAUA CACAGGGG
	2190	UUCUGGAG	CUGAUGA	Х	GAA	AUUUCUUC	GAAGAAAUC CUCCAGAA
	2193	UUCUUCUG	CUGAUGA	X	GAA	AGGAUUUC	GAAAUCCUC CAGAAGAA
20	2208	CUGAUUGU	CUGAUGA	Х	GAA	AUUUCUUU	AAAGAAAUU ACAAUCAG
	2209	UCUGAUUG	CUGAUGA	Х	GAA	AAUUUCUU	AAGAAAUUA CAAUCAGA
	2214	UGAUCUCU	CUGAUGA	X	GAA	AUUGUAAU	AUUACAAUC AGAGAUCA
	2221					AUCUCUGA	UCAGAGAUC AGGAAGCA
	2234	GCAGGAGG	CUGAUGA	X	GAA	AUGGUGCU	AGCACCAUA CCUCCUGC
25	2238					AGGUAUGG	
	2250					AGGUUUCG	CGAAACCUC AGUGAUCA
	2257					AUCACUGA	UCAGUGAUC ACACAGUG
	2271					AUGGCCAC	GUGGCCAUC AGCAGUUC
	2278					ACUGCUGA	UCAGCAGUU CCACCACU
30	2279					AACUGCUG	CAGCAGUUC CACCACUU
	2287					AGUGGUGG	
	2288					AAGUGGUG	
	2289	UGACAGUC '	CUGAUGA :	X	GAA	AAAGUGGU	ACCACUUUA GACUGUCA

	2296	AUUAGCAU	CUGAUGA	Х	GAA	ACAGUCUA	UAGACUGUC	AUGCUAAU
	2302	GACACCAU	CUGAUGA	X	GAA	AGCAUGAC	GUCAUGCUA	AUGGUGUC
	2310	GGCUCGGG	CUGAUGA	X	GAA	ACACCAUU	AAUGGUGUC	CCCGAGCC
	2320	AGUGAUCU	CUGAUGA	Х	GAA	AGGCUCGG	CCGAGCCUC	AGAUCACU
5	2325	AACCAAGU	CUGAUGA	X	GAA	AUCUGAGG	CCUCAGAUC	ACUUGGUU
	2329	UUUAAACC	CUGAUGA	X	GAA	AGUGAUCU	AGAUCACUU	GGUUUAAA
	2333	UGUUUUUA	CUGAUGA	X	GAA	ACCAAGUG	CACUUGGUU	UAAAAACA
	2334	UUGUUUUU	CUGAUGA	X	GAA	AACCAAGU	ACUUGGUUU	AAAAACAA
	2335	GUUGUUUU	CUGAUGA	X	GAA	AAACCAAG	CUUGGUUUA	AAAACAAC
10	2352	UCUUGUUG	CUGAUGA	Х	GAA	AUUUUGUG	CACAAAAUA	CAACAAGA
	2370	CCUAAAAU	CUGAUGA	Х	GAA	AUUCCAGG	CCUGGAAUU	AUUUUAGG
	2371	UCCUAAAA	CUGAUGA	Х	GAA	AAUUCCAG	CUGGAAUUA	UUUUAGGA
	2373	GGUCCUAA	CUGAUGA	X	GAA	AUAAUUCC	GGAAUUAUU	UUAGGACC
	2374	UGGUCCUA	CUGAUGA	Х	GAA	AAUAAUUC	GAAUUAUUU	UAGGACCA
15	2375	CUGGUCCU	CUGAUGA	X	GAA	AAAUAAUU	UUUUUAUUAA	AGGACCAG
	2376	CCUGGUCC	CUGAUGA	X	GAA	AAAAUAAU	AUUUUUUA	GGACCAGG
	2399	UUUCAAUA	CUGAUGA	X	GAA	ACAGCGUG	CACGCUGUU	UAUUGAAA
	2400	CUUUCAAU	CUGAUGA	X	GAA	AACAGCGU	ACGCUGUUU	AUUGAAAG
	2401	UCUUUCAA	CUGAUGA	X	GAA	AAACAGCG	CGCUGUUUA	UUGAAAGA
20	2403	ACUCUUUC	CUGAUGA	Х	GAA	AUAAACAG	CUGUUUAUU	GAAAGAGU
	2412	UCUUCUGU	CUGAUGA	Х	GAA	ACUCUUUC	GAAAGAGUC	ACAGAAGA
	2433	CAGUGAUA	CUGAUGA	X	GAA	ACACCUUC	GAAGGUGUC	UAUCACUG
	2435	UGCAGUGA	CUGAUGA	Х	GAA	AGACACCU	AGGUGUCUA	UCACUGCA
	2437	UUUGCAGU	CUGAUGA	Х	GAA	AUAGACAC	GUGUCUAUC	ACUGCAAA
25	2465	UUUCCACA	CUGAUGA	X	GAA	AGCCCUUC	GAAGGGCUC	UGUGGAAA
	2476	GUAUGC UG	CUGAUGA	X	GAA	ACUUUCCA	UGGAAAGUU	CAGCAUAC
	2477	GGUAUGCU	CUGAUGA	X	GAA	AACUUUCC	GGAAAGUUC	AGCAUACC
	2483	CAGUGAGG	CUGAUGA	X	GAA	AUGCUGAA	UUCAGCAUA	CCUCACUG
	2487	UGAACAGU	CUGAUGA	Х	GAA	AGGUAUGC	GCAUACCUC	ACUGUUCA
30	2493	GUUCCUUG	CUGAUGA	Х	GAA	ACAGUGAG	CUCACUGUU	CAAGGAAC
	2494	GGUUCCUU	CUGAUGA	X	GAA	AACAGUGA	UCACUGUUC	AAGGAACC
	2504	ACUUGUCC	CUGAUGA	X	GAA	AGGUUCCU	AGGAACCUC	GGACAAGU
	2513	CCAGAUUA	CUGAUGA	X	GAA	ACUUGUCC	GGACAAGUC	UAAUCUGG

	2515	CUCCAGA	J CUGAUGA	. >	(GA)	A AGACUUGU	ACAAGUCUA	AUCUGGAG
	2518	CAGCUCCA	CUGAUGA	. >	GA/	A AUUAGACU	AGUCUAAUC	UGGAGCUG
	2529	GUUAGAGU	J CUGAUGA	. Х	GA.	AUCAGCUC	GAGCUGAUC	ACUCUAAC
	2533	GCAUGUUA	CUGAUGA	. X	GAA	AGUGAUCA	UGAUCACUC	UAACAUGC
5	2535	GUGCAUGU	J CUGAUGA	. X	GA	AGAGUGAU	AUCACUCUA	ACAUGCAC
	2560	CCAGAAGA	CUGAUGA	X	GAA	AGUCGCAG	CUGCGACUC	UCUUCUGG
	2562	AGCCAGAA	CUGAUGA	Х	GAA	AGAGUCGC	GCGACUCUC	UUCUGGCU
	2564	GGAGCCAG	CUGAUGA	Х	GAA	AGAGAGUC	GACUCUCUU	CUGGCUCC
	2565	AGGAGCCA	CUGAUGA	Х	GAA	AAGAGAGU	ACUCUCUUC	UGGCUCCU
10	2571	GUUAAUAG	CUGAUGA	X	GAA	AGCCAGAA	UUCUGGCUC	CUAUUAAC
	2574	AGGGUUAA	CUGAUGA	X	GAA	AGGAGCCA	UGGCUCCUA	UUAACCCU
	25 76	GGAGGGUU	CUGAUGA	Х	GAA	AUAGGAGC	GCUCCUAUU	AACCCUCC
	2577	AGGAGGGU	CUGAUGA	X	GAA	AAUAGGAG	CUCCUAUUA	ACCCUCCU
	2583	CGGAUAAG	CUGAUGA	X	GAA	AGGGUUAA	UUAACCCUC	CUUAUCCG
15	2586	UUUCGGAU	CUGAUGA	X	GAA	AGGAGGGU	ACCCUCCUU	AUCCGAAA
	2587	UUUUCGGA	CUGAUGA	X	GAA	AAGGAGGG	CCCUCCUUA	UCCGAAAA
	258 9	AUUUUUCG	CUGAUGA	Х	GAA	AUAAGGAG	CUCCUUAUC	CGAAAAAU
	2606	CAGAAGAA	CUGAUGA	X	GAA	ACCUUUUC	GAAAAGGUC	UUCUUCUG
	2608	UUCAGAAG	CUGAUGA	Х	GAA	AGACCUUU	AAAGGUCUU	CUUCUGAA
20	2609	UUUCAGAA	CUGAUGA	Х	GAA	AAGACCUU	AAGGUCUUC	UUCUGAAA
	2611	UAUUUCAG	CUGAUGA	X	GAA	AGAAGACC	GGUCUUCUU	CUGAAAUA
	2612	UUAUUUCA	CUGAUGA	X	GAA	AAGAAGAC	GUCUUCUUC I	UGAAAUAA
	2619	UCAGUCUU	CUGAUGA	X	GAA	AUUUCAGA	UCUGAAAUA 2	AAGACUGA
	2630	UUGAUAGG	CUGAUGA	X	GAA	AGUCAGUC	GACUGACUA (CCUAUCAA
25	2634	AUAAUUGA	CUGAUGA	X	GAA	AGGUAGUC	GACUACCUA (JCAAUUAU
	2636	UUAUAAUU	CUGAUGA	X	GAA	AUAGGUAG	CUACCUAUC A	AAUUAUAA
	2640	UCCAUUAU	CUGAUGA	X	GAA	AUUGAUAG	CUAUCAAUU A	AUAAUGGA
	2641	GUCCAUUA	CUGAUGA	X	GAA	AAUUGAUA	UAUCAAUUA (JAAUGGAC
	2643	GGGUCCAU	CUGAUGA	X	GAA	AUAAUUGA	UCAAUUAUA A	UGGACCC
30	2661	UCCAAAGG	CUGAUGA	X	GAA	ACUUCAUC	GAUGAAGUU C	CUUUGGA
	2662	AUCCAAAG	CUGAUGA	X	GAA	AACUUCAU	AUGAAGUUC C	UUUGGAU
	2665	CUCAUCCA	CUGAUGA :	X	GAA	AGGAACUU	AAGUUCCUU U	IGGAUGAG
	2666	GCUCAUCC	CUGAUGA :	X ·	GAA	AAGGAACU	AGUUCCUUU G	GAUGAGC

	2000	OCAUAAGG	COGAOGA	Λ	GAA	AGCCGCUC	GAGCGGCUC	CCUUAUGA
	2692	GGCAUCAU	CUGAUGA	X	GAA	AGGGAGCC	GGCUCCCUU	AUGAUGCO
	2693	UGGCAUCA	CUGAUGA	x	GAA	AAGGGAGC	GCUCCCUUA	UGAUGCCA
	2714	CCCGGGCA	CUGAUGA	x	GAA	ACUCCCAC	GUGGGAGUU	UGCCCGGG
5	2715	UCCCGGGC	CUGAUGA	X	GAA	AACUCCCA	UGGGAGUUU	GCCCGGGA
	2730	CCCAGUUU	CUGAUGA	x	GAA	AGUCUCUC	GAGAGACUU	AAACUGGG
	2731	GCCCAGUU	CUGAUGA	x	GAA	AAGUCUCU	AGAGACUUA	AACUGGGC
	2744	UUCCAAGU	CUGAUGA	X	GAA	AUUUGCCC	GGGCAAAUC	ACUUGGAA
	2748	CCUCUUCC	CUGAUGA	X	GAA	AGUGAUUU	AAAUCACUU	GGAAGAGG
10	2761	UUUUCCAA	CUGAUGA	Х	GAA	AGCCCCUC	GAGGGGCUU	UUGGAAAA
	2762	CUUUUCCA	CUGAUGA	Х	GAA	AAGCCCCU	AGGGGCUUU	UGGAAAAG
	2763	ACUUUUCC	CUGAUGA	x	GAA	AAAGCCCC	GGGGCUUUU	GGAAAAGU
	2775	GAUGCUUG	CUGAUGA	Х	GAA	ACCACUUU	AAAGUGGUU	CAAGCAUC
	2 7 76	UGAUGCUU	CUGAUGA	x	GAA	AACCACUU	AAGUGGUUC	AAGCAUCA
15	2783	CAAAUGCU	CUGAUGA	X	GAA	AUGCUUGA	UCAAGCAUC	AGCAUUUG
	2789	UAAUGCCA	CUGAUGA	X	GAA	AUGCUGAU	AUCAGCAUU	UGGCAUUA
	2790	UUAAUGCC	CUGAUGA	Х	GAA	AAUGCUGA	UCAGCAUUU	GGCAUUAA
	2796	GAUUUCUU	CUGAUGA	X	GAA	AUGCCAAA	UUUGGCAUU	AAGAAAUC
	2797	UGAUUUCU	CUGAUGA	x	GAA	AAUGCCAA	UUGGCAUUA	AGAAAUCA
20	2804	ACGUAGGU	CUGAUGA	Х	GAA	AUUUCUUA	UAAGAAAUC	ACCUACGU
	28 09	CCGGCACG	CUGAUGA	x	GAA	AGGUGAUU	AAUCACCUA	CGUGCCGG
	2864	GAGCUUUG	CUGAUGA	Х	GAA	ACUCGCUG	CAGCGAGUA	CAAAGCUC
	2872	AGUCAUCA	CUGAUGA	Х	GAA	AGCUUUGU	ACAAAGCUC	UGAUGACU
	2886	AAGAUUUU	CUGAUGA	Х	GAA	AGCUCAGU	ACUGAGCUA	AAAAUCUU
25	2892	UGGGUCAA	CUGAUGA	х	GAA	AUUUUUAG	CUAAAAAUC	UUGACCCA
	2894	UGUGGGUC	CUGAUGA	Х	GAA	AGAUUUUU	AAAAAUCUU	GACCCACA
	2904	UGGUGGCC	CUGAUGA	x	GAA	AUGUGGGU	ACCCACAUU	GGCCACCA
	2914	CACGUUCA	CUGAUGA	X	GAA	AUGGUGGC	GCCACCAUC	UGAACGUG
	292 5	AGCAGGUU	CUGAUGA	X	GAA	ACCACGUU	AACGUGGUU	AACCUGCU
30	2926	CAGCAGGU	CUGAUGA	X	GAA	AACCACGU	ACGUGGUUA	ACCUGCUG
	2962	CACCAUCA	CUGAUGA	X	GAA	AGGCCCUC	GAGGGCCUC	UGAUGGUG
	2973	UAUUCAAC	CUGAUGA	X	GAA	AUCACCAU	AUGGUGAUU	GUUGAAUA
	2976	CAGUAUUC	CUGAUGA	Х	GAA	ACAAUÇAC	GUGAUUGUU	GAAUACUG

	2981	AUUUGCAG	CUGAUGA	. X	GAA	AUUCAACA	UGUUGAAUA	CUGCAAAU
	29 90	GAUUUCCA	CUGAUGA	X	GAA	AUUUGCAG	CUGCAAAUA	UGGAAAUC
	2998	GUUGGAGA	CUGAUGA	X	GAA	AUUUCCAU	AUGGAAAUC	UCUCCAAC
	3000	UAGUUGGA	CUGAUGA	X	GAA	AGAUUUCC	GGAAAUCUC	UCCAACUA
5	3002	GGUAGUUG	CUGAUGA	X	GAA	AGAGAUUU	AAAUCUCUC	CAACUACC
	3008	UCUUGAGG	CUGAUGA	X	GAA	AGUUGGAG	CUCCAACUA	CCUCAAGA
	3012	UUGCUCUU	CUGAUGA	Х	GAA	AGGUAGUU	AACUACCUC	AAGAGCAA
	3029	GAAAAAAU	CUGAUGA	х	GAA	AGUCACGU	ACGUGACUU	AUUUUUUC
	3030	AGAAAAA	CUGAUGA	х	GAA	AAGUCACG	CGUGACUUA	ບບບບບບ
10	3032	UGAGAAAA	CUGAUGA	Х	GAA	AUAAGUCA	UGACUUAUU	UUUUCUCA
	3033	UUGAGAAA	CUGAUGA	Х	GAA	AAUAAGUC	GACUUAUUU	UUUCUCAA
	3034	GUUGAGAA	CUGAUGA	Х	GAA	AAAUAAGU	ACUUAUUUU	UUCUCAAC
	3035	UGUUGAGA	CUGAUGA	x	GAA	AAAAUAAG	CUUAUUUUU	UCUCAACA
	3036	UUGUUGAG	CUGAUGA	х	GAA	AAAAAUAA	UUUUUUAUU	CUCAACAA
15	3037	CUUGUUGA	CUGAUGA	Х	GAA	AAAAAUA	UAUUUUUUC	UCAACAAG
	3039	uccuuguu	CUGAUGA	х	GAA	AGAAAAA	ບບບບບບ cuc	AACAAGGA
	3057	UCCAUGUG	CUGAUGA	Х	GAA	AGUGCUGC	GCAGCACUA	CACAUGGA
	3070	υυςυυυςυ	CUGAUGA	х	GAA	AGGCUCCA	UGGAGCCUA	AGAAAGAA
	3120	ACGCUAUC	CUGAUGA	х	GAA	AGUCUUGG	CCAAGACUA	GAUAGCGU
20	3124	GGUGACGC	CUGAUGA	х	GAA	AUCUAGUC	GACUAGAUA	GCGUCACC
	3129	CUGCUGGU	CUGAUGA	x	GAA	ACGCUAUC	GAUAGCGUC	ACCAGCAG
	3146	AGCUCGCA	CUGAUGA	x	GAA	AGCUUUCG	CGAAAGCUU	UGCGAGCU
	3147	GAGCUCGC	CUGAUGA	Х	GAA	AAGCUUUC	GAAAGCUUU	GCGAGCUC
	3155	GAAAGCCG	CUGAUGA	X	GAA	AGCUCGCA	UGCGAGCUC	CGGCUUUC
25	3161	CUUCCUGA	CUGAUGA	х	GAA	AGCCGGAG	CUCCGGCUU	UCAGGAAG
	3162	UCUUCCUG	CUGAUGA	x	GAA	AAGCCGGA	uccgccuuu	CAGGAAGA
	3163	AUCUUCCU	CUGAUGA	х	GAA	AAAGCCGG	ccgcuuuc .	AGGAAGAU
	3172	CAGACUUU	CUGAUGA	х	GAA	AUCUUCCU	AGGAAGAUA .	AAAGUCUG
	3178	AUCACUCA	CUGAUGA	X	GAA	ACUUUUAU	AUAAAAGUC	UGAGUGAU
30	3189	UCUUCCUC	CUGAUGA	X	GAA	ACAUCACU	AGUGAUGUU (GAGGAAGA
	3205	ACCGUCAG	CUGAUGA	X	GAA	AUCCUCCU	AGGAGGAUU (CUGACGGU
	3206	AACCGUCA	CUGAUGA	x	GAA	AAUCCUCC	GGAGGAUUC 1	JGACGGUU
	3214	CUUGUAGA	CUGAUGA	Х	GAA	ACCGUCAG	CUGACGGUU 1	JCUACAAG

	3215	CCOOGOAG	CUGAUGA	X	GAA	AACCGUCA	UGACGGUUU	CUACAAGG
	3216	UCCUUGUA	CUGAUGA	X	GAA	AAACCGUC	GACGGUUUC	UACAAGGA
	3218	GCUCCUUG	CUGAUGA	X	GAA	AGAAACCG	CGGUUUCUA	CAAGGAGC
	3231	UCCAUAGU	CUGAUGA	X	GAA	AUGGGCUC	GAGCCCAUC	ACUAUGGA
5	3235	AUCUUCCA	CUGAUGA	х	GAA	AGUGAUGG	CCAUCACUA	UGGAAGAU
	3244	AGAAAUCA	CUGAUGA	x	GAA	AUCUUCCA	UGGAAGAUC	UGAUUUCU
	3249	CUGUAAGA	CUGAUGA	x	GAA	AUCAGAUC	GAUCUGAUU	UCUUACAG
	3250	ACUGUAAG	CUGAUGA	Х	GAA	AAUCAGAU	AUCUGAUUU	CUUACAGU
	3251	AACUGUAA	CUGAUGA	х	GAA	AAAUCAGA	UCUGAUUUC	UUACAGUU
10	3253	AAAACUGU	CUGAUGA	х	GAA	AGAAAUCA	UGAUUUCUU	ACAGUUUU
	3254	GAAAACUG	CUGAUGA	х	GAA	AAGAAAUC	GAUUUCUUA	CAGUUUUC
	3259	CACUUGAA	CUGAUGA	х	GAA	ACUGUAAG	CUUACAGUU	UUCAAGUG
	3260	CCACUUGA	CUGAUGA	X	GAA	AACUGUAA	UUACAGUUU	UCAAGUGG
	3261	GCCACUUG	CUGAUGA	X	GAA	AAACUGUA	UACAGUUUU	CAAGUGGC
15	3262	GGCCACUU	CUGAUGA	Х	GAA	AAAACUGU	ACAGUUUUC	AAGUGGCC
	3284	AAGACAGG	CUGAUGA	Х	GAA	ACUCCAUG	CAUGGAGUU	ccugucuu
	3285	GAAGACAG	CUGAUGA	х	GAA	AACUCCAU	AUGGAGUUC	CUGUCUUC
	3290	UUCUGGAA	CUGAUGA	X	GAA	ACAGGAAC	GUUCCUGUC	UUCCAGAA
	3292	CUUUCUGG	CUGAUGA	X	GAA	AGACAGGA	UCCUGUCUU	CCAGAAAG
20	329 3	ACUUUCUG	CUGAUGA	X	GAA	AAGACAGG	CCUGUCUUC	CAGAAAGU
	3306	UCCCGAUG	CUGAUGA	X	GAA	AUGCACUU	AAGUGCAUU	CAUCGGGA
	3307	GUCCCGAU	CUGAUGA	Х	GAA	AAUGCACU	AGUGCAUUC	AUCGGGAC
	3310	CAGGUCCC	CUGAUGA	X	GAA	AUGAAUGC	GCAUUCAUC	GGGACCUG
	333 3	GAUAAAAG	CUGAUGA	X	GAA	AUGUUUCU	AGAAACAUU	CUUUUAUC
25	3334	AGAUAAAA	CUGAUGA	X	GAA	AAUGUUUC	GAAACAUUC	UUUUAUCU
	3336	UCAGAUAA	CUGAUGA	X	GAA	AGAAUGUU	AACAUUCUU	UUAUCUGA
	3337	CUCAGAUA	CUGAUGA	Х	GAA	AAGAAUGU	ACAUUCUUU	UAUCUGAG
	3338	UCUCAGAU	CUGAUGA	Х	GAA	AAAGAAUG	CAUUCUUUU	AUCUGAGA
	33 39	UUCUCAGA	CUGAUGA	X	GAA	AAAAGAAU	AUUCUUUUA	UCUGAGAA
30	3341	UGUUCUCA	CUGAUGA	X	GAA	AUAAAAGA	UCUUUUAUC	UGAGAACA
	33 63	AAAUCACA	CUGAUGA	X	GAA	AUCUUCAC	GUGAAGAUU	UGUGAUUU
	3364	AAAAUCAC	CUGAUGA	X	GAA	AAUCUUCA	UGAAGAUUU	GUGAUUUU
	3370	AAGGCCAA	CUGAUGA	Х	GAA	AUCACAAA	UUUGUGAUU	uuggccuu

	33/1	CAAGGCC	A CUGAUG!	4 2	(GA	A AAUCACAA	UUGUGAUUU	UGGCCUUG
	3372	GCAAGGC	CUGAUGA	A 3	GA.	A AAAUCACA	UGUGAUUUU	GGCCUUGC
	3378	UCCCGGG	CUGAUGA	Α >	GA	A AGGCCAAA	uuuggccuu	GCCCGGGA
	3388	CUUAUAA	A CUGAUGA	λ)	GA	A AUCCCGGG	CCCGGGAUA	UUUAUAAG
5	3390	UUCUUAU	A CUGAUGA	X X	GA/	A AUAUCCCG	CGGGAUAUU	UAUAAGAA
	3391	GUUCUUA	J CUGAUGA	X	GA/	A AAUAUCCC	GGGAUAUUU	AUAAGAAC
	3392	GGUUCUUA	A CUGAUGA	X	GA/	AAAUAUCC	GGAUAUUUA	UAAGAACC
	3394	GGGGUUCU	J CUGAUGA	X	GAZ	NAUAAAUA	AUAUUUAUA	AGAACCCC
	3406	UCUCACAU	CUGAUGA	. X	GAZ	AUCGGGGU	ACCCCGAUU	AUGUGAGA
10	3407	UUCUCACA	CUGAUGA	. X	GAA	AAUCGGGG	CCCCGAUUA	UGUGAGAA
	3424	AAGUCGAG	CUGAUGA	Х	GAA	AUCUCCUU	AAGGAGAUA	CUCGACUU
	3427	AGGAAGUC	CUGAUGA	Х	GAA	AGUAUCUC	GAGAUACUC	GACUUCCU
	3432	UUCAGAGG	CUGAUGA	Х	GAA	AGUCGAGU	ACUCGACUU	CCUCUGAA
	3433	UUUCAGAG	CUGAUGA	Х	GAA	AAGUCGAG	CUCGACUUC	CUCUGAAA
15	3436	CCAUUUCA	CUGAUGA	Х	GAA	AGGAAGUC	GACUUCCUC	UGAAAUGG
	3451	AGAUUCGG	CUGAUGA	X	GAA	AGCCAUCC	GGAUGGCUC	CCGAAUCU
	3458	CAAAGAUA	CUGAUGA	Х	GAA	AUUCGGGA	UCCCGAAUC	UAUCUUUG
	3460	GUCAAAGA	CUGAUGA	X	GAA	AGAUUCGG	CCGAAUCUA	UCUUUGAC
	3462	UUGUCAAA	CUGAUGA	X	GAA	AUAGAUUC	GAAUCUAUC	UUUGACAA
20	3464	UUUUGUCA	CUGAUGA	X	GAA	AGAUAGAU	AUCUAUCUU	UGACAAAA
	3465	AUUUUGUC	CUGAUGA	Х	GAA	AAGAUAGA	UCUAUCUUU (GACAAAAU
	3474	GUGCUGUA	CUGAUGA	Х	GAA	AUUUUGUC	GACAAAAUC 1	UACAGCAC
	3476	UGGUGCUG	CUGAUGA	X	GAA	AGAUUUUG	CAAAAUCUA (CÁGCACCA
	3500					ACCACACG	CGUGUGGUC t	JUACGGAG
25	3502	UACUCCGU	CUGAUGA	X	GAA	AGACCACA	UGUGGUCUU A	ACGGAGUA
	3503	AUACUCCG	CUGAUGA	X	GAA	AAGACCAC	GUGGUCUUA (CGGAGUAU
	3510	CACAGCAA	CUGAUGA	X	GAA	ACUCCGUA	UACGGAGUA U	JUGCUGUG
	3512	CCCACAGC	CUGAUGA	X	GAA	AUACUCCG	CGGAGUAUU C	CUGUGGG
	3525	AAGGAGAA	CUGAUGA	X	GAA	AUUUCCCA	UGGGAAAUC L	ນເດເດດ
30	3527					AGAUUUCC	GGAAAUCUU C	CUCCUUAG
	3528	CCUAAGGA					GAAAUCUUC U	ICCUUAGG
	3530						AAUCUUCUC C	UUAGGUG
	3533	ACCCACCU	CUGAUGA	X	GAA	AGGAGAAG	CUUCUCCUU A	GGUGGGU

	3534	GACCCACC	CUGAUGA	Х	GAA	AAGGAGAA	UUCUCCUUA	GGUGGGUC
	3542	GGUAUGGA	CUGAUGA	X	GAA	ACCCACCU	AGGUGGGUC	UCCAUACC
	3544	UGGGUAUG	CUGAUGA	Х	GAA	AGACCCAC	GUGGGUCUC	CAUACCCA
	3548	CUCCUGGG	CUGAUGA	X	GAA	AUGGAGAC	GUCUCCAUA	CCCAGGAG
5	3558	UCCAUUUG	CUGAUGA	X	GAA	ACUCCUGG	CCAGGAGUA	CAAAUGGA
	3575	GACUGCAA	CUGAUGA	X	GAA	AGUCCUCA	UGAGGACUU	UUGCAGUC
	3576	CGACUGCA	CUGAUGA	Х	GAA	AAGUCCUC	GAGGACUUU	UGCAGUCG
	3577	GCGACUGC	CUGAUGA	X	GAA	AAAGUCCU	AGGACUUUU	GCAGUCGC
	3583	CCUCAGGC	CUGAUGA	Х	GAA	ACUGC AA A	UUUGCAGUC	GCCUGAGG
10	3613	GUACUCAG	CUGAUGA	Х	GAA	AGCUCUCA	UGAGAGCUC	CUGAGUAC
	3620	GAGUAGAG	CUGAUGA	Х	GAA	ACUCAGGA	UCCUGAGUA	CUCUACUC
	3623	CAGGAGUA	CUGAUGA	Х	GAA	AGUACUCA	UGAGUACUC	UACUCCUG
	3625	UUCAGGAG	CUGAUGA	Х	GAA	AGAGUACU	AGUACUCUA	CUCCUGAA
	3628	GAUUUCAG	CUGAUGA	Х	GAA	AGUAGAGU	ACUCUACUC	CUGAAAUC
15	3636	AUCUGAUA	CUGAUGA	X	GAA	AUUUCAGG	CCUGAAAUC	UAUCAGAU
	3638	UGAUCUGA	CUGAUGA	Х	GAA	AGAUUUCA	UGAAAUCUA	UCAGAUCA
	3640	CAUGAUCU	CUGAUGA	Х	GAA	AUAGAUUU	AAAUCUAUC	AGAUCAUG
	3645	UCCAGCAU	CUGAUGA	Х	GAA	AUCUGAUA	UAUCAGAUC	AUGCUGGA
	3689	GUUCUGCA	CUGAUGA	Х	GAA	AUCUUGGC	GCCAAGAUU	UGCAGAAC
20	3690	AGUUCUGC	CUGAUGA	Х	GAA	AAUCUUGG	CCAAGAUUU	GCAGAACU
	3699	UUUUCCAC	CUGAUGA	X	GAA	AGUUCUGC	GCAGAACUU	GUGGAAAA
	3711	AAAUCACC	CUGAUGA	х	GAA	AGUUUUUC	GAAAAACUA	GGUGAUUU
	3718	UUGAAGCA	CUGAUGA	X	GAA	AUCACCUA	UAGGUGAUU	UGCUUCAA
	3719	CUUGAAGC	CUGAUGA	х	GAA	AAUCACCU	AGGUGAUUU	GCUUCAAG
25	3723	UUUGCUUG	CUGAUGA	X	GAA	AGCAAAUC	GAUUUGCUU	CAAGCAAA
	3724	AUUUGCUU	CUGAUGA	X	GAA	AAGCAAAU	AUUUGCUUC	AAGCAAAU
	3735	UCCUGUUG	CUGAUGA	Х	GAA	ACAUUUGC	GCAAAUGUA	CAACAGGA
	3748	GUAGUCUU	CUGAUGA	Х	GAA	ACCAUCCU	AGGAUGGUA	AAGACUAC
	3755	UUGGGAUG	CUGAUGA	X	GAA	AGUCUUUA	UAAAGACUA	CAUCCCAA
30	3759	UUGAUUGG	CUGAUGA	X	GAA	AUGUAGUC	GACUACAUC	CCAAUCAA
	3765	AUGGCAUU	CUGAUGA	Х	GAA	AUUGGGAU	AUCCCAAUC	AAUGCCAU
	3774	CCUGUCAG	CUGAUGA	X	GAA	AUGGCAUU	AAUGCCAUA	CUGACAGG
	3787	AAACCCAC	CUGAUGA	Х	GAA	AUUUCCUG	CAGGAAAUA	GUGGGUUU

	3794	AGUAUGUA	CUGAUGA	X	GAA	ACCCACUA	UAGUGGGUU UACAUACU
	3795	GAGUAUGL	J CUGAUGA	X	GA.	AACCCACU	AGUGGGUUU ACAUACUC
	3796	UGAGUAUG	CUGAUGA	. х	GAA	AAACCCAC	GUGGGUUUA CAUACUCA
	3800	GAGUUGAG	G CUGAUGA	. х	GAA	AUGUAAAC	GUUUACAUA CUCAACUC
5	3803	CAGGAGUU	J CUGAUGA	. X	GAA	AGUAUGUA	UACAUACUC AACUCCUG
	3808	GAAGGCAG	CUGAUGA	. X	GAA	AGUUGAGU	ACUCAACUC CUGCCUUC
	3815	CCUCAGAG	CUGAUGA	X	GAA	AGGCAGGA	UCCUGCCUU CUCUGAGG
	3816	UCCUCAGA	CUGAUGA	X	GAA	AAGGCAGG	CCUGCCUUC UCUGAGGA
	3818	AGUCCUCA	CUGAUGA	Х	GAA	AGAAGGCA	UGCCUUCUC UGAGGACU
10	3827	CCUUGAAG	CUGAUGA	Х	GAA	AGUCCUCA	UGAGGACUU CUUCAAGG
	3828	UCCUUGAA	CUGAUGA	X	GAA	AAGUCCUC	GAGGACUUC UUCAAGGA
	3830	UUUCCUUG	CUGAUGA	Х	GAA	AGAAGUCC	GGACUUCUU CAAGGAAA
	3831	cuuuccuu	CUGAUGA	X	GAA	AAGAAGUC	GACUUCUUC AAGGAAAG
	3841	AGCUGAAA	CUGAUGA	X	GAA	ACUUUCCU	AGGAAAGUA UUUCAGCU
15	3843	GGAGCUGA	CUGAUGA	X	GAA	AUACUUUC	GAAAGUAUU UCAGCUCC
	3844	CGGAGCUG	CUGAUGA	X	GAA	AAUACUUU	AAAGUAUUU CAGCUCCG
	3845	UCGGAGCU	CUGAUGA	Х	GAA	AAAUACUU	AAGUAUUUC AGCUCCGA
	3850	AAACUUCG	CUGAUGA	Х	GAA	AGCUGAAA	UUUCAGCUC CGAAGUUU
	3857	CUGAAUUA	CUGAUGA	X	GAA	ACUUCGGA	UCCGAAGUU UAAUUCAG
20	3858	CCUGAAUU	CUGAUGA	X	GAA	AACUUCGG	CCGAAGUUU AAUUCAGG
	3859	UCCUGAAU	CUGAUGA	X	GAA	AAACUUCG	CGAAGUUUA AUUCAGGA
	3862	GCUUCCUG	CUGAUGA	Х	GAA	AUUAAACU	AGUUUAAUU CAGGAAGC
	3863	AGCUUCCU	CUGAUGA	Х	GAA	AAUUAAAC	GUUUAAUUC AGGAAGCU
	3872	CAUCAUCA	CUGAUGA	Х	GAA	AGCUUCCU	AGGAAGCUC UGAUGAUG
25	3882	ACAUAUCU	CUGAUGA	X	GAA	ACAUCAUC	GAUGAUGUC AGAUAUGU
	3887	CAUUUACA	CUGAUGA	X	GAA	AUCUGACA	UGUCAGAUA UGUAAAUG
	3891	AAAGCAUU	CUGAUGA	X	GAA	ACAUAUCU	AGAUAUGUA AAUGCUUU
	3898	GAACUUGA	CUGAUGA	X	GAA	AGCAUUUA	UAAAUGCUU UCAAGUUC
	3899	UGAACUUG	CUGAUGA	X	GAA	AAGCAUUU	AAAUGCUUU CAAGUUCA
30	3900	AUGAACUU	CUGAUGA	X	GAA	AAAGCAUU	AAUGCUUUC AAGUUCAU
	3905	GGCUCAUG	CUGAUGA	X	GAA	ACUUGAAA	UUUCAAGUU CAUGAGCC
	3906	AGGCUCAU	CUGAUGA	X	GAA	AACUUGAA	UUCAAGUUC AUGAGCCU
	3924	AAGGUUUU	CUGAUGA	X	GAA	AUUCUUUC	GAAAGAAUC AAAACCUU

	3932	GUUCUUCA	CUGAUGA	X	GAA	AGGUUUUG	CAAAACCUU	UGAAGAAC
	3933	AGUUCUUC	CUGAUGA	Х	GAA	AAGGUUUU	AAAACCUUU	GAAGAACU
	3942	UUCGGUAA	CUGAUGA	X	GAA	AGUUCUUC	GAAGAACUU	UUACCGAA
	3943	AUUCGGUA	CUGAUGA	X	GAA	AAGUUCUU	AAGAACUUU	UACCGAAU
5	3944	CAUUCGGU	CUGAUGA	X	GAA	AAAGUUCU	AGAACUUUU	ACCGAAUG
	3945	GCAUUCGG	CUGAUGA	X	GAA	AAAAGUUC	GAACUUUUA	CCGAAUGC
	3 9 59	CAAACAUG	CUGAUGA	X	GAA	AGGUGGCA	UGCCACCUC	CAUGUUUG
	3965	AGUCAUCA	CUGAUGA	X	GAA	ACAUGGAG	CUCCAUGUU	UGAUGACU
	3966	UAGUCAUC	CUGAUGA	Х	GAA	AACAUGGA	UCCAUGUUU	GAUGACUA
10	3974	CGCCCUGG	CUGAUGA	X	GAA	AGUCAUCA	UGAUGACUA	CCAGGGCG
	3994	GGCCAACA	CUGAUGA	X	GAA	AGUGCUGC	GCAGCACUC	UGUUGGCC
	3998	GAGAGGCC	CUGAUGA	X	GAA	ACAGAGUG	CACUCUGUU	GGCCUCUC
	4004	GCAUGGGA	CUGAUGA	X	GAA	AGGCCAAC	GUUGGCCUC	UCCCAUGC
	4006	CAGCAUGG	CUGAUGA	X	GAA	AGAGGCCA	UGGCCUCUC	CCAUGCUG
15	4022	UCCAGGUG	CUGAUGA	Х	GAA	AGCGCUUC	GAAGCGCUU	CACCUGGA
	4023	GUCCAGGU	CUGAUGA	X	GAA	AAGCGCUU	AAGCGCUUC	ACCUGGAC
	4052	UCUUGAGC	CUGAUGA	X	GAA	AGGCCUUG	CAAGGCCUC	GCUCAAGA
	4056	UCAAUCUU	CUGAUGA	X	GAA	AGCGAGGC	GCCUCGCUC	AAGAUUGA
	4062	CUCAAGUC	CUGAUGA	X	GAA	AUCUUGAG	CUCAAGAUU	GACUUGAG
20	4067	UUACUCUC	CUGAUGA	X	GAA	AGUCAAUC	GAUUGACUU	GAGAGUAA
	4074	UUACUGGU	CUGAUGA	X	GAA	ACUCUCAA	UUGAGAGUA	ACCAGUAA
	4081	CUUACUUU	CUGAUGA	X	GAA	ACUGGUUA	UAACCAGUA	AAAGUAAG
	4087	CGACUCCU	CUGAUGA	X	GAA	ACUUUUAC	GUAAAAGUA	AGGAGUCG
	4094	ACAGCCCC	CUGAUGA	X	GAA	ACUCCUUA	UAAGGAGUC	GGGGCUGU
25	4103	UGACAUCA	CUGAUGA	X	GAA	ACAGCCCC	GGGGCUGUC	UGAUGUCA
	4110	GGCCUGCU	CUGAUGA	X	GAA	ACAUCAGA	UCUGAUGUC	AGCAGGCC
	4123	AUGGCAGA	CUGAUGA	X	GAA	ACUGGGCC	GGCCCAGUU	UCUGCCAU
	4124	AAUGGCAG	CUGAUGA	X	GAA	AACUGGGC	GCCCAGUUU	CUGCCAUU
	4125	GAAUGGCA	CUGAUGA	X	GAA	AAACUGGG	CCCAGUUUC	UGCCAUUC
30	4132	ACAGCUGG	CUGAUGA	X	GAA	AUGGCAGA	UCUGCCAUU	CCAGCUGU
	4133	CACAGCUG	CUGAUGA	X	GAA	AAUGGCAG	CUGCCAUUC	CAGCUGUG
	4149	CCUUCGCU	CUGAUGA	Х	GAA	ACGUGCCC	GGGCACGUC	AGCGAAGG
	4169	CGUAGGUG	CUGAUGA	Х	GAA	ACCUGCGC	GCGCAGGUU	CACCUACG

...

	4170	UCGUAGGU	CUGAUGA	. }	(GAA	AACCUGCG	CGCAGGUUC ACCUACGA
	4175	CGUGGUCG	CUGAUGA	. >	GAA	AGGUGAAC	GUUCACCUA CGACCACG
	4203	CAGCACGC	CUGAUGA	X	GAA	AUUUUCCU	AGGAAAAUC GCGUGCUG
	4214	GGGGCGGG	CUGAUGA	. Х	GAA	AGCAGCAC	GUGCUGCUC CCCGCCCC
5	4229	CCGAGUUG	CUGAUGA	. Х	GAA	AGUCUGGG	CCCAGACUA CAACUCGG
	4235	GGACCACC	CUGAUGA	. X	GAA	AGUUGUAG	CUACAACUC GGUGGUCC
	4242	GAGUACAG	CUGAUGA	. X	GAA	ACCACCGA	UCGGUGGUC CUGUACUC
	4247	GGGUGGAG	CUGAUGA	X	GAA	ACAGGACC	GGUCCUGUA CUCCACCC
	4250	GUGGGGUG	CUGAUGA	Х	GAA	AGUACAGG	CCUGUACUC CACCCCAC
10	42 63	AAACUCUA	CUGAUGA	Х	GAA	AUGGGUGG	CCACCCAUC UAGAGUUU
	4265	UCAAACUC	CUGAUGA	Х	GAA	AGAUGGGU	ACCCAUCUA GAGUUUGA
	4270	UCGUGUCA	CUGAUGA	Х	GAA	ACUCUAGA	UCUAGAGUU UGACACGA
	4271	UUCGUGUC	CUGAUGA	X	GAA	AACUCUAG	CUAGAGUUU GACACGAA
	4284	CUAGAAAU	CUGAUGA	X	GAA	AGGCUUCG	CGAAGCCUU AUUUCUAG
15	4285	UCUAGAAA	CUGAUGA	X	GAA	AAGGCUUC	GAAGCCUUA UUUCUAGA
	4287	CUUCUAGA	CUGAUGA	X	GAA	AUAAGGCU	AGCCUUAUU UCUAGAAG
	4288	GCUUCUAG	CUGAUGA	X	GAA	AAUAAGGC	GCCUUAUUU CUAGAAGC
	4289	UGCUUCUA	CUGAUGA	Х	GAA	AAAUAAGG	CCUUAUUUC UAGAAGCA
	4291	UGUGCUUC	CUGAUGA	X	GAA	AGAAAUAA	UUAUUUCUA GAAGCACA
20	4305	GGUAUAAA	CUGAUGA	X	GAA	ACACAUGU	ACAUGUGUA UUUAUACC
	4307	GGGGUAUA	CUGAUGA	X	GAA	AUACACAU	AUGUGUAUU UAUACCCC
	4308	GGGGGUAU	CUGAUGA	X	GAA	AAUACACA	UGUGUAUUU AUACCCCC
	4309	UGGGGGUA	CUGAUGA	X	GAA	AAAUACAC	GUGUAUUUA UACCCCCA
	4311	CCUGGGGG	CUGAUGA	X	GAA	AUAAAUAC	GUAUUUAUA CCCCCAGG
25	4325	GCAAAAGC	CUGAUGA	X	GAA	AGUUUCCU	AGGAAACUA GCUUUUGC
	4329					AGCUAGUU	AACUAGCUU UUGCCAGU
	4330	UACUGGCA	CUGAUGA	X	GAA	AAGCUAGU	ACUAGCUUU UGCCAGUA
	4331	AUACUGGC	CUGAUGA	Х	GAA	AAAGCUAG	CUAGCUUUU GCCAGUAU
	4338	AUGCAUAA	CUGAUGA	Х	GAA	ACUGGCAA	UUGCCAGUA UUAUGCAU
30	4340	AUAUGCAU	CUGAUGA	X	GAA	AUACUGGC	GCCAGUAUU AUGCAUAU
	4341	•				AAUACUGG	
	4347					AUGCAUAA	
	4349	UAAACUUA	CUGAUGA	X	GAA	AUAUGCAU	AUGCAUAUA UAAGUUUA

	4351	UGUAAACU	CUGAUGA	A	GAA	AUAUAUGC	GCAUAUAUA	AGUUUACA
	4355	AAGGUGUA	CUGAUGA	х	GAA	ACUUAUAU	AUAUAAGUU	UACACCUU
	4356	AAAGGUGU	CUGAUGA	x	GAA	AACUUAUA	UAUAAGUUU	ACACCUUU
	4357	UAAAGGUG	CUGAUGA	x	GAA	AAACUUAU	AUAAGUUUA	CACCUUUA
5	4363	GAAAGAUA	CUGAUGA	Х	GAA	AGGUGUAA	UUACACCUU	UAUCUUUC
	4364	GGAAAGAU	CUGAUGA	X	GAA	AAGGUGUA	UACACCUUU	AUCUUUCC
	4365	UGGAAAGA	CUGAUGA	Х	GAA	AAAGGUGU	ACACCUUUA	UCUUUCCA
	4367	CAUGGAAA	CUGAUGA	Х	GAA	AUAAAGGU	ACCUUUAUC	UUUCCAUG
	4369	CCCAUGGA	CUGAUGA	x	GAA	AGAUAAAG	CUUUAUCUU	UCCAUGGG
10	4370	UCCCAUGG	CUGAUGA	X	GAA	AAGAUAAA	UUUAUCUUU	CCAUGGGA
	4371	CUCCCAUG	CUGAUGA	Х	GAA	AAAGAUAA	UUAUCUUUC	CAUGGGAG
	4389	AUCACAAA	CUGAUGA	X	GAA	AGCAGCUG	CAGCUGCUU	UUUGUGAU
	4390	AAUCACAA	CUGAUGA	x	GAA	AAGCAGCU	AGCUGCUUU	UUGUGAUU
	4391	AAAUCACA	CUGAUGA	x	GAA	AAAGCAGC	GCUGCUUUU	UGUGAUUU
15	4392	AAAAUCAC	CUGAUGA	x	GAA	AAAAGCAG	CUGCUUUUU	GUGAUUUU
	4398	AAAAAUUA	CUGAUGA	x	GAA	AUCACAAA	UUUGUGAUU	UULUUUAAU
	4399	UAUUAAAA	CUGAUGA	X	GAA	AAUCACAA	UUGUGAUUU	AUAAUUU
	4400	CUAUUAAA	CUGAUGA	х	GAA	AAAUCACA	UGUGAUUUU	UUUAAUAG
	4401	ACUAUUAA	CUGAUGA	Х	GAA	AAAAUCAC	GUGAUUUUU	UUAAUAGU
20	4402	CACUAUUA	CUGAUGA	X	GAA	AAAAAUCA	UGAUUUUUU	UAAUAGUG
	4403	GCACUAUU	CUGAUGA	х	GAA	AAAAAAUC	GAUUUUUUU	AAUAGUGC
	4404	AGCACUAU	CUGAUGA	X	GAA	UAAAAAA	AUUUUUUUA	AUAGUGCU
	4407	AAAAGCAC	CUGAUGA	X	GAA	AAAAUUA	AUAAUUUU	GUGCUUUU
	4413	AAAAAAA	CUGAUGA	X	GAA	AGCACUAU	AUAGUGCUU	טטטטטטטט
25	4414	AAAAAAA	CUGAUGA	х	GAA	AAGCACUA	UAGUGCUUU	טטטטטטטט
	4415	САААААА	CUGAUGA	X	GAA	AAAGCACU	AGUGCUUUU	บบบบบบบ
	4416	UCAAAAAA	CUGAUGA	x	GAA	AAAAGCAC	GUGCUUUUU	UUUUUUGA
	4417	GUCAAAAA	CUGAUGA	х	GAA	AAAAAGCA	ugcuuuuuu	UUUUUGAC
	4418	AGUCAAAA	CUGAUGA	x	GAA	AAAAAAGC	GCUUUUUUU	UUUUGACU
30	4419	UAGUCAAA	CUGAUGA	x	GAA	AAAAAAG	cuuuuuuu	UUUGACUA
	4420	UUAGUCAA	CUGAUGA	X	GAA	AAAAAAA	บบบบบบบบบ	UUGACUAA
	4421	GUUAGUCA	CUGAUGA	x	GAA	AAAAAA	บบบบบบบบบ	UGACUAAC
							טטטטטטטטט	

	4427	AUUCUUGU	CUGAUGA	Х	GAA	AGUCAAAA	UUUUGACUA ACAAGAAU
	4438	UCUGGAGU	CUGAUGA	Х	GAA	ACAUUCUU	AAGAAUGUA ACUCCAGA
	4442	UCUAUCUG	CUGAUGA	Х	GAA	AGUUACAU	AUGUAACUC CAGAUAGA
	4448	UAUUUCUC	CUGAUGA	Х	GAA	AUCUGGAG	CUCCAGAUA GAGAAAUA
5	4456	CUUGUCAC	CUGAUGA	X	GAA	AUUUCUCU	AGAGAAAUA GUGACAAG
	4476	UUUAGCAG	CUGAUGA	X	GAA	AGUGUUCU	AGAACACUA CUGCUAAA
	4482	UGAGGAUU	CUGAUGA	X	GAA	AGCAGUAG	CUACUGCUA AAUCCUCA
	4486	AACAUGAG	CUGAUGA	X	GAA	AUUUAGCA	UGCUAAAUC CUCAUGUU
	4489	AGUAACAU	CUGAUGA	X	GAA	AGGAUUUA	UAAAUCCUC AUGUUACU
10	4494	CACUGAGU	CUGAUGA	X	GAA	ACAUGAGG	CCUCAUGUU ACUCAGUG
	4495	ACACUGAG	CUGAUGA	Х	GAA	AACAUGAG	CUCAUGUUA CUCAGUGU
	4498	CUAACACU	CUGAUGA	Х	GAA	AGUAACAU	AUGUUACUC AGUGUUAG
	4504	AUUUCUCU	CUGAUGA	X	GAA	ACACUGAG	CUCAGUGUU AGAGAAAU
	4505	GAUUUCUC	CUGAUGA	X	GAA	AACACUGA	UCAGUGUUA GAGAAAUC
15	451 3	UUAGGAAG	CUGAUGA	X	GAA	AUUUCUCU	AGAGAAAUC CUUCCUAA
	451 6	GGUUUAGG	CUGAUGA	X	GAA	AGGAUUUC	GAAAUCCUU CCUAAACC
	4517	GGGUUUAG	CUGAUGA	X	GAA	AAGGAUUU	AAAUCCUUC CUAAACCC
	4520	AUUGGGUU	CUGAUGA	Х	GAA	AGGAAGGA	UCCUUCCUA AACCCAAU
	453 3	GAGCAGGG	CUGAUGA	X	GAA	AGUCAUUG	CAAUGACUU CCCUGCUC
20	4534	GGAGCAGG	CUGAUGA	X	GAA	AAGUCAUU	AAUGACUUC CCUGCUCC
	4541	GGGGGUUG	CUGAUGA	X	GAA	AGCAGGGA	UCCCUGCUC CAACCCCC
	4557	CGUGCCCU	CUGAUGA	X	GAA	AGGUGGCG	CGCCACCUC AGGGCACG
	4576	CUCAAUCA	CUGAUGA	X	GAA	ACUGGUCC	GGACCAGUU UGAUUGAG
	4577	CCUCAAUC	CUGAUGA	Х	GAA	AACUGGUC	GACCAGUUU GAUUGAGG
25	4581	AGCUCCUC	CUGAUGA	X	GAA	AUCAAACU	AGUUUGAUU GAGGAGCU
	4598	CAUUGGGU	CUGAUGA	X	GAA	AUCAGUGC	GCACUGAUC ACCCAAUG
	4610	GGGUACGU	CUGAUGA	X	GAA	AUGCAUUG	CAAUGCAUC ACGUACCC
	4615	CAGUGGGG	CUGAUGA	Х	GAA	ACGUGAUG	CAUCACGUA CCCCACUG
	4664	CUGGGGCU	CUGAUGA	Х	GAA	ACGGGCUU	AAGCCCGUU AGCCCCAG
30	4665	CCUGGGGC	CUGAUGA	X	GAA	AACGGGCU	AGCCCGUUA GCCCCAGG
	4678	CAGCCAGU	CUGAUGA	X	GAA	AUCCCCUG	CAGGGGAUC ACUGGCUG
	4700	ACUCCCGA	CUGAUGA	X	GAA	AUGUUGCU	AGCAACAUC UCGGGAGU
	4702	GGACUCCC	CUGAUGA	X	GAA	AGAUGUUG	CAACAUCUC GGGAGUCC

	4709	UGCUAGAG	CUGAUGA	Х	GAA	ACUCCCGA	UCGGGAGUC	CUCUAGCA
	4712	GCCUGCUA	CUGAUGA	X	GAA	AGGACUCC	GGAGUCCUC	UAGCAGGC
	4714	AGGCCUGC	CUGAUGA	X	GAA	AGAGGACU	AGUCCUCUA	GCAGGCCU
	4723	ACAUGUCU	CUGAUGA	Х	GAA	AGGCCUGC	GCAGGCCUA	AGACAUGU
5	4802	GCGUCUCA	CUGAUGA	X	GAA	AUUCUUUC	GAAAGAAUU	UGAGACGC
	4803	UGCGUCUC	CUGAUGA	X	GAA	AAUUCUUU	AAAGAAUUU	GAGACGCA
	4840	GCAUUGCU	CUGAUGA	Х	GAA	AGCCCCGU	ACGGGGCUC	AGCAAUGC
	4852	GCCACUGA	CUGAUGA	X	GAA	AUGGCAUU	AAUGCCAUU	UCAGUGGC
	4853	AGCCACUG	CUGAUGA	х	GAA	AAUGGCAU	AUGCCAUUU	CAGUGGCU
10	4854	AAGCCACU	CUGAUGA	Х	GAA	AAAUGGCA	UGCCAUUUC	AGUGGCUU
	4862	GAGCUGGG	CUGAUGA	Х	GAA	AGCCACUG	CAGUGGCUU	CCCAGCUC
	4863	AGAGCUGG	CUGAUGA	х	GAA	AAGCCACU	AGUGGCUUC	CCAGCUCU
	4870	AAGGGUCA	CUGAUGA	x	GAA	AGCUGGGA	UCCCAGCUC	UGACCCUU
	4878	AAAUGUAG	CUGAUGA	х	GAA	AGGGUCAG	CUGACCCUU	CUACAUUU
15	4879	CAAAUGUA	CUGAUGA	Х	GAA	AAGGGUCA	UGACCCUUC	UACAUUUG
	4881	CUCAAAUG	CUGAUGA	Х	GAA	AGAAGGGU	ACCCUUCUA	CAUUUGAG
	4885	GGCCCUCA	CUGAUGA	X	GAA	AUGUAGAA	UUCUACAUU	UGAGGGCC
	4886	GGGCCCUC	CUGAUGA	X	GAA	AAUGUAGA	UCUACAUUU	GAGGGCCC
	4929	AUCCAGAA	CUGAUGA	Х	GAA	AUGUCCCC	GGGGACAUU	UUCUGGAU
20	4930	AAUCCAGA	CUGAUGA	Х	GAA	AAUGUCCC	GGGACAUUU	UCUGGAUU
	4931	GAAUCCAG	CUGAUGA	Х	GAA	AAAUGUCC	GGACAUUUU	CUGGAUUC
-	4932	AGAAUCCA	CUGAUGA	Х	GAA	AAAAUGUC	GACAUUUUC	UGGAUUCU
	4938	CCUCCCAG	CUGAUGA	X	GAA	AUCCAGAA	UUCUGGAUU	CUGGGAGG
	4939	GCCUCCCA	CUGAUGA	Х	GAA	AAUCCAGA	UCUGGAUUC	UGGGAGGC
25	4963	AAAAAAGA	CUGAUGA	X	GAA	AUUUGUCC	GGACAAAUA	טכטטטטטט
	4965	CCAAAAAA	CUGAUGA	x	GAA	AUAUUUGU	ACAAAUAUC	บบบบบบเร
	4967	UUCCAAAA	CUGAUGA	Х	GAA	AGAUAUUU	AAAUAUCUU	UUUUGGAA
	4968	GUUCCAAA	CUGAUGA	Х	GAA	AAGAUAUU	AAUAUCUUU	UUUGGAAC
	4969	AGUUCCAA	CUGAUGA	X	GAA	AAAGAUAU	AUAUCUUUU	UUGGAACU
30	4970	UAGUUCCA	CUGAUGA	Х	GAA	AAAAGAUA	UAUCUUUUU	UGGAACUA
	4971					AAAAGAU		
	4978	•				AGUUCCAA		
	4987	AGGUCUAA	CUGAUGA	Х	GAA	AUUUGCUU	AAGCAAAUU	UUAGACCU

	4988	AAGGUCUA	A CUGAUGA	. 2	(GA	A AAUUUGCU	AGCAAAUUU UAGACCUU
	498 9	AAAGGUCI	J CUGAUGA		(GA)	A AAAUUUGC	GCAAAUUUU AGACCUUU
	4990	UAAAGGU	CUGAUGA	. 3	(GA	A AAAAUUUG	CAAAUUUUA GACCUUUA
	4996	CAUAGGUA	CUGAUGA	. 3	GAA	A AGGUCUAA	UUAGACCUU UACCUAUG
5	4997	CCAUAGGU	CUGAUGA	. }	GA	AAGGUCUA	UAGACCUUU ACCUAUGG
	4998	UCCAUAGO	CUGAUGA	. >	GA,	AAAGGUCU	AGACCUUUA CCUAUGGA
	5002	CACUUCCA	CUGAUGA		GAA	AGGUAAAG	CUUUACCUA UGGAAGUG
	5013	GGACAUAG	CUGAUGA	X	GAA	ACCACUUC	GAAGUGGUU CUAUGUCC
	5014	UGGACAUA	CUGAUGA	X	GAA	AACCACUU	AAGUGGUUC UAUGUCCA
10	5016	AAUGGACA	CUGAUGA	X	GAA	AGAACCAC	GUGGUUCUA UGUCCAUU
	5020	UGAGAAUG	CUGAUGA	X	GAA	ACAUAGAA	UUCUAUGUC CAUUCUCA
	5024	CGAAUGAG	CUGAUGA	X	GAA	AUGGACAU	AUGUCCAUU CUCAUUCG
	5025	ACGAAUGA	CUGAUGA	X	GAA	AAUGGACA	UGUCCAUUC UCAUUCGU
	5027	CCACGAAU	CUGAUGA	X	GAA	AGAAUGGA	UCCAUUCUC AUUCGUGG
15	5030	AUGCCACG	CUGAUGA	X	GAA	AUGAGAAU	AUUCUCAUU CGUGGCAU
	5031	CAUGCCAC	CUGAUGA	Х	GAA	AAUGAGAA	UUCUCAUUC GUGGCAUG
	5041	CAAAUCAA	CUGAUGA	Х	GAA	ACAUGCCA	UGGCAUGUU UUGAUUUG
	5042	ACAAAUCA	CUGAUGA	Х	GAA	AACAUGCC	GGCAUGUUU UGAUUUGU
	5043	UACAAAUC	CUGAUGA	X	GAA	AAACAUGC	GCAUGUUUU GAUUUGUA
20	5047	GUGCUACA	CUGAUGA	X	GAA	AUCAAAAC	GUUUUGAUU UGUAGCAC
	5048	AGUGCUAC	CUGAUGA	Х	GAA	AAUCAAAA	UUUUGAUUU GUAGCACU
	5051	CUCAGUGC	CUGAUGA	Х	GAA	ACAAAUCA	UGAUUUGUA GCACUGAG
	5069	UCAGAGUU	CUGAUGA	Х	GAA	AGUGCCAC	GUGGCACUC AACUCUGA
	5074	UGGGCUCA	CUGAUGA	X	GAA	AGUUGAGU	ACUCAACUC UGAGCCCA
25	5084	GCCAAAAG	CUGAUGA	X	GAA	AUGGGCUC	GAGCCCAUA CUUUUGGC
	5087	GGAGCCAA	CUGAUGA	X	GAA	AGUAUGGG	CCCAUACUU UUGGCUCC
	5088	AGGAGCCA	CUGAUGA	X	GAA	AAGUAUGG	CCAUACUUU UGGCUCCU
	5089	GAGGAGCC	CUGAUGA	X	GAA	AAAGUAUG	CAUACUUUU GGCUCCUC
	5094	UACUAGAG	CUGAUGA	X	GAA	AGCCAAAA	UUUUGGCUC CUCUAGUA
30	5097	UCUUACUA	CUGAUGA	X	GAA	AGGAGCCA	UGGCUCCUC UAGUAAGA
	5099	CAUCUUAC	CUGAUGA	X	GAA	AGAGGAGC	GCUCCUCUA GUAAGAUG
	5102	GUGCAUCU	CUGAUGA	X	GAA	ACUAGAGG	CCUCUAGUA AGAUGCAC
	5119	CUCUGGCU	CUGAUGA	X	GAA	AGUUUUCA	UGAAAACUU AGCCAGAG

	5120	ACUCUGGC	CUGAUGA	X	GAA	AAGUUUUC	GAAAACUUA	GCCAGAGU
	5129	GACAACCU	CUGAUGA	Х	GAA	ACUCUGGC	GCCAGAGUU	AGGUUGUC
	5130	AGACAACC	CUGAUGA	х	GAA	AACUCUGG	CCAGAGUUA	GGUUGUCU
	5134	CUGGAGAC	CUGAUGA	х	GAA	ACCUAACU	AGUUAGGUU	GUCUCCAG
5	5137	GGCCUGGA	CUGAUGA	х	GAA	ACAACCUA	UAGGUUGUC	UCCAGGCC
	5139	AUGGCCUG	CUGAUGA	х	GAA	AGACAACC	GGUUGUCUC	CAGGCCAU
	5156	UUCAGUGU	CUGAUGA	x	GAA	AGGCCAUC	GAUGGCCUU	ACACUGAA
	5157	UUUCAGUG	CUGAUGA	X	GAA	AAGGCCAU	AUGGCCUUA	CACUGAAA
	5170	UAGAAUGU	CUGAUGA	X	GAA	ACAUUUUC	GAAAAUGUC	ACAUUCUA
10	5175	CAAAAUAG	CUGAUGA	Х	GAA	AUGUGACA	UGUCACAUU	CUAUUUUG
	5176	CCAAAAUA	CUGAUGA	Х	GAA	AAUGUGAC	GUCACAUUC	UAUUUUGG
	5178	ACCCAAAA	CUGAUGA	x	GAA	AGAAUGUG	CACAUUCUA	UUUUGGGU
	5180	AUACCCAA	CUGAUGA	х	GAA	AUAGAAUG	CAUUCUAUU	UUGGGUAU
	5181	AAUACCCA	CUGAUGA	Х	GAA	AAUAGAAU	AUUCUAUUU	UGGGUAUU
15	5182	UAAUACCC	CUGAUGA	Х	GAA	AAAUAGAA	UUCUAUUUU	GGGUAUUA
	5187	AAUUAUAA	CUGAUGA	Х	GAA	ACCCAAAA	UUUUGGGUA	AUAAUAUA
	5189	UUAUAUAU	CUGAUGA	х	GAA	AUACCCAA	UUGGGUAUU	AAUAUAUA
	5190	CUAUAUAU	CUGAUGA	х	GAA	AAUACCCA	UGGGUAUUA	AUAUAUAG
	5193	GGACUAUA	CUGAUGA	Х	GAA	AUUAAUAC	GUAUUAAUA	UAUAGUCC
20	5195	CUGGACUA	CUGAUGA	Х	GAA	AUAUUAAU	AUUAAUAUA	UAGUCCAG
	5197	GUCUGGAC	CUGAUGA	Х	GAA	AUAUAUUA	UAAUAUAUA	GUCCAGAC
	5200	AGUGUCUG	CUGAUGA	Х	GAA	ACUAUAUA	UAUAUAGUC	CAGACACU
	5209	AUUGAGUU	CUGAUGA	X	GAA	AGUGUCUG	CAGACACUU	AACUCAAU
	5210	AAUUGAGU	CUGAUGA	X	GAA	AAGUGUCU	AGACACUUA	ACUCAAUU
2 5	5214	AAGAAAUU	CUGAUGA	Х	GAA	AGUUAAGU	ACUUAACUC	AAUUUCUU
	5218	UACCAAGA	CUGAUGA	Х	GAA	AUUGAGUU	AACUCAAUU	UCUUGGUA
	5219	AUACCAAG	CUGAUGA	X	GAA	AAUUGAGU	ACUCAAUUU	CUUGGUAU
	5220	AAUACCAA	CUGAUGA	Х	GAA	AAAUUGAG	CUCAAUUUC	UUGGUAUU
	5222	AUAAUACC	CUGAUGA	X	GAA	AGAAAUUG	CAAUUUCUU	GGUAUUAU
30	5226	CAGAAUAA	CUGAUGA	Х	GAA	ACCAAGAA	UUCUUGGUA	UUAUUCUG
						AUACCAAG		
	5229	AAACAGAA	CUGAUGA	X	GAA	AAUACCAA	UUGGUAUUA	UUCUGUUU
	5231	CAAAACAG	CUGAUGA	Х	GAA	AUAAUACC	GGUAUUAUU	CUGUUUUG

	5232						AAUAAUAC	GUAUUAUUC	uguuuugo
	5236						ACAGAAUA	UAUUCUGUU	UUGCACAG
	5237						AACAGAAU	AUUCUGUUU	UGCACAGU
•	5238	AACUGUG	C CUGAUG	Α :	X GA	λA	AAACAGAA	UUCUGUUUU	GCACAGUU
5	5246	UCACAACI	J CUGAUGA	A :	X GA	λA	ACUGUGCA	UGCACAGUU	AGUUGUGA
	5247	UUCACAA	CUGAUGA	A :	X GA	ŁΑ	AACUGUGC	GCACAGUUA	GUUGUGAA
	5250	UCUUUCA	CUGAUG!	A 2	X GA	A.	ACUAACUG	CAGUUAGUU	GUGAAAGA
	5284	CUCCUCAC	G CUGAUGA	A 2	X GA	L A	ACUGCAUU	AAUGCAGUC	CUGAGGAG
	5296	AUGGAGA	CUGAUGA	A 2	K GA	ιA	ACUCUCCU	AGGAGAGUU	UUCUCCAU
10	5297	UAUGGAGA	CUGAUGA	λ >	GA.	A	AACUCUCC	GGAGAGUUU	UCUCCAUA
	5298	AUAUGGAG	CUGAUGA	. Σ	(GA	ιA.	AAACUCUC	GAGAGUUUU	CUCCAUAU
	529 9	GAUAUGGA	CUGAUGA	X	GA	Α.	AAAACUCU	AGAGUUUUC	UCCAUAUC
	5301	UUGAUAUG	CUGAUGA	. Х	GA.	Α.	AGAAAACU	AGUUUUCUC	CAUAUCAA
	5305	CGUUUUGA	CUGAUGA	. х	GA.	A	AUGGAGAA	UUCUCCAUA	UCAAAACG
15	5307	CUCGUUUU	CUGAUGA	X	GA.	A i	AUAUGGAG	CUCCAUAUC	AAAACGAG
	5336	ACCUUAUU	CUGAUGA	X	GA.	A A	ACCUUUUU	AAAAAGGUC	AAUAAGGU
	5340	CUUGACCU	CUGAUGA	Х	GAA	A A	AUUGACCU	AGGUCAAUA	AGGUCAAG
	5345	CUUCCCUU	CUGAUGA	Х	GAZ	A A	ACCUU AU U	AAUAAGGUC	AAGGGA A G
	5361	GGUAUAGA	CUGAUGA	Х	GAA	A A	ACGGGGUC	GACCCCGUC	UCUAUACC
20	5363	UUGGUAUA	CUGAUGA	Χ	GAA	4 <i>F</i>	AGACGGGG	CCCCGUCUC	UAUACCAA
	5365	GGUUGGUA	CUGAUGA	X,	GAA	A A	AGAGACGG	CCGUCUCUA	UACCAACC
	5367	UUGGUUGG	CUGAUGA	Х	GAA	A A	AUAGAGAC	GUCUCUAUA	CCAACCAA
	5382	UGUUGGUG	CUGAUGA	Х	GAA	\ A	UUGGUUU	AAACCAAUU	CACCAACA
	5383	GUGUUGGU	CUGAUGA	X	GAA	A A	AUUGGUU	AACCAAUUC Z	ACCAACAC
2 5	5395.	UGGGUCCC	CUGAUGA	X	GAA	A A	CUGUGUU	AACACAGUU (GGACCCA
	5417	ACGUGACU	CUGAUGA	X	GAA	. A	CUUCCUG	CAGGAAGUC A	AGUCACGU
	5421	GGAAACGU	CUGAUGA	Х	GAA	A	.CUGACUU	AAGUCAGUC A	ACGUUUCC
	5426	GAAAAGGA	CUGAUGA	Х	GAA	. A	CGUGACU	AGUCACGUU t	JCCUUUUC
	5427	UGAAAAGG	CUGAUGA	х	GAA	A	ACGUGAC	GUCACGUUU (CUUUUCA
30	5428	AUGAAAAG	CUGAUGA	Х	GAA	. A.	AACGUGA	UCACGUUUC C	
	5431	UAAAUGAA	CUGAUGA	Х	GAA	. A	GGAAACG	cgบบบccบบ ບ	
	5432	UUAAAUGA	CUGAUGA	X	GAA	A	AGGAAAC	GUUUCCUUU U	
	5433	AUUAAAUG	CUGAUGA	X	GAA	A.	AAGGAAA	ນນນດດນນນນ ດ	AUUUAAU

WO 97/15662 PCT/US96/17480

	5434	CAUUAAAU	CUGAUGA	Х	GAA	AAAAGGAA	υυςςυυυυς	AUUUAAUG
	5437	CCCCAUUA	CUGAUGA	X	GAA	AUGAAAAG	CUUUUCAUU	UAAUGGGG
	5438	UCCCCAUU	CUGAUGA	x	GAA	AAUGAAAA	UUUUCAUUU	AAUGGGGA
	5439	AUCCCCAU	CUGAUGA	X	GAA	AAAUGAAA	UUUCAUUUA	AUGGGGAU
5	5448	GAUAGUGG	CUGAUGA	х	GAA	AUCCCCAU	AUGGGGAUU	CCACUAUC
	5449	AGAUAGUG	CUGAUGA	x	GAA	AAUCCCCA	UGGGGAUUC	CACUAUCU
	5454	GUGUGAGA	CUGAUGA	Х	GAA	AGUGGAAU	AUUCCACUA	UCUCACAC
	5456	UAGUGUGA	CUGAUGA	Х	GAA	AUAGUGGA	UCCACUAUC	UCACACUA
	5458	AUUAGUGU	CUGAUGA	Х	GAA	AGAUAGUG	CACUAUCUC	ACACUAAU
10	5464	UUUCAGAU	CUGAUGA	Х	GAA	AGUGUGAG	CUCACACUA	AUCUGAAA
	5467	UCCUUUCA	CUGAUGA	Х	GAA	AUUAGUGU	ACACUAAUC	UGAAAGGA
	5489	CGCCAGCU	CUGAUGA	Х	GAA	AUGCUCUU	AAGAGCAUU	AGCUGGCG
	549 0	GCGCCAGC	CUGAUGA	X	GAA	AAUGCUCU	AGAGCAUUA	GCUGGCGC
	5501	GUGCUUAA	CUGAUGA	х	GAA	AUGCGCCA	UGGCGCAUA	UUAAGCAC
15	5503	AAGUGCUU	CUGAUGA	х	GAA	AUAUGCGC	GCGCAUAUU	AAGCACUU
	5504	AAAGUGCU	CUGAUGA	х	GAA	AAUAUGCG	CGCAUAUUA	AGCACUUU
	5511	GGAGCUUA	CUGAUGA	X	GAA	AGUGCUUA	UAAGCACUU	UAAGCUCC
	5512	AGGAGCUU	CUGAUGA	Х	GAA	AAGUGCUU	AAGCACUUU	AAGCUCCU
	5513	AAGGAGCU	CUGAUGA	X	GAA	AAAGUGCU	AGCACUUUA	AGCUCCUU
20	5518	UACUCAAG	CUGAUGA	Х	GAA	AGCUUAAA	UUUAAGCUC	CUUGAGUA
	5521	UUUUACUC	CUGAUGA	Х	GAA	AGGAGCUU	AAGCUCCUU	GAGUAAAA
	5526	CACCUUUU	CUGAUGA	Х	GAA	ACUCAAGG	CCUUGAGUA	AAAAGGUG
	5537	AAAUUACA	CUGAUGA	х	GAA	ACCACCUU	AAGGUGGUA	UGUAAUUU
	5541	GCAUAAAU	CUGAUGA	Х	GAA	ACAUACCA	UGGUAUGUA	AUUUAUGC
25	5544	CUUGCAUA	CUGAUGA	Х	GAA	AUUACAUA	UAUGUAAUU	UAUGCAAG
	5545	CCUUGCAU	CUGAUGA	X	GAA	AAUUACAU	AUGUAAUUU	AUGCAAGG
	554 6	ACCUUGCA	CUGAUGA	Х	GAA	AAAUUACA	UGUAAUUUA	UGCAAGGU
	555 5	UGGAGAAA	CUGAUGA	X	GAA	ACCUUGCA	UGCAAGGUA	UUUCUCCA
	5557	ACUGGAGA	CUGAUGA	Х	GAA	AUACCUUG	CAAGGUAUU	UCUCCAGU
30	5558	AACUGGAG	CUGAUGA	Х	GAA	AAUACCUU	AAGGUAUUU	CUCCAGUU
	5559					AAAUACCU	-	UCCAGUUG
	5561					AGAAAUAC		CAGUUGGG
	5566	UGAGUCCC	CUGAUGA	Х	GAA	ACUGGAGA	UCUCCAGUU	GGGACUCA

	5573	3 AAUAUCCU	CUGAUGA	Х	GAA	AGUCCCAA	UUGGGACUC AGGAUAUU
	5579	UUAACUAA	CUGAUGA	Х	GAA	AUCCUGAG	CUCAGGAUA UUAGUUAA
	5581	CAUUAACU	CUGAUGA	X	GAA	AUAUCCUG	CAGGAUAUU AGUUAAUG
	5582	UCAUUAAC	CUGAUGA	Х	GAA	AAUAUCCU	AGGAUAUUA GUUAAUGA
5	5585	GGCUCAUU	CUGAUGA	X (GAA	ACUAAUAU	AUAUUAGUU AAUGAGCC
	5586	UGGCUCAU	CUGAUGA	х	GAA	AACUAAUA	UAUUAGUUA AUGAGCCA
	5596	CUUCUAGU	CUGAUGA	х	GAA	AUGGCUCA	UGAGCCAUC ACUAGAAG
	5600	UUUUCUUC	CUGAUGA	х	GAA	AGUGAUGG	CCAUCACUA GAAGAAAA
	5615	CAGUUGAA	CUGAUGA	х	GAA	AUGGGCUU	AAGCCCAUU UUCAACUG
10	561 6	GCAGUUGA	CUGAUGA	х	GAA	AAUGGGCU	AGCCCAUUU UCAACUGC
	5617	AGCAGUUG	CUGAUGA	х	GAA .	AAAUGGGC	GCCCAUUUU CAACUGCU
	5618	AAGCAGUU	CUGAUGA	X G	GAA .	AAAAUGGG	CCCAUUUUC AACUGCUU
	5626	AAGUUUCA	CUGAUGA	ХС	SAA .	AGCAGUUG	CAACUGCUU UGAAACUU
	5627	CAAGUUUC	CUGAUGA	X G	AA A	AAGCAGUU	AACUGCUUU GAAACUUG
15	5634	CCCCAGGC	CUGAUGA	ХG	AA A	AGUUUCAA	UUGAAACUU GCCUGGGG
	5644	CAUGCUCA	CUGAUGA	X G	AA A	ACCCCAGG	CCUGGGGUC UGAGCAUG
	5661	UGUCUCCC (CUGAUGA	X G	AA A	AUUCCCAU	AUGGGAAUA GGGAGACA
	5674	CCCUUUCC (CUGAUGA	X G	AA A	ACCCUGUC	GACAGGGUA GGAAAGGG
	568 8	CUGAAGAG (CUGAUGA	X G	AA A	AGGCGCCC	GGGCGCCUA CUCUUCAG
20	5691	ACCCUGAA (CUGAUGA	X G.	AA A	AGUAGGCG	CGCCUACUC UUCAGGGU
	5693	AGACCCUG C	TUGAUGA	X G	AA A	GAGUAGG	CCUACUCUU CAGGGUCU
	5694	UAGACCCU C	UGAUGA 2	K GZ	AA A	AGAGUAG	CUACUCUUC AGGGUCUA
	5700	GAUCUUUA C					UUCAGGGUC UAAAGAUC
	5702	UUGAUCUU C					CAGGGUCUA AAGAUCAA
25		GCCCACUU C					CUAAAGAUC AAGUGGGC
	5719	AGCGAUCC C					GUGGGCCUU GGAUCGCU
	5724	AGCUUAGC C					CCUUGGAUC GCUAAGCU
	5728	AGCCAGCU C					GGAUCGCUA AGCUGGCU
	5737	AUCAAACA C					AGCUGGCUC UGUUUGAU
30	5741	UAGCAUCA CI					GGCUCUGUU UGAUGCUA
	5742	AUAGCAUC C					GCUCUGUUU GAUGCUAU
	574 9	UGCAUAAA CI					UUGAUGCUA UUUAUGCA
	5751	CUUGCAUA CI	JGAUGA X	GA	JA A	JAGCAUC	GAUGCUAUU UAUGCAAG

	5752	ACUUGCAU	CUGAUGA	X	GAA	AAUAGCAU	AUGCUAUUU	AUGCAAGU
	5753	AACUUGCA	CUGAUGA	x	GAA	AAAUAGCA	UGCUAUUUA	UGCAAGUU
	5761	UAGACCCU	CUGAUGA	X	GAA	ACUUGCAU	AUGCAAGUU	AGGGUCUA
	5762	AUAGACCC	CUGAUGA	X	GAA	AACUUGCA	UGCAAGUUA	GGGUCUAU
5	5767	AAUACAUA	CUGAUGA	X	GAA	ACCCUAAC	GUUAGGGUC	UAUGUAUU
	5769	UAAAUACA	CUGAUGA	Х	GAA	AGACCCUA	UAGGGUCUA	UGUAUUUA
	5773	AUCCUAAA	CUGAUGA	X	GAA	ACAUAGAC	GUCUAUGUA	UUUAGGAU
	5775	GCAUCCUA	CUGAUGA	x	GAA	AUACAUAG	CUAUGUAUU	UAGGAUGC
	5776	CGCAUCCU	CUGAUGA	Х	GAA	AAUACAUA	UAUGUAUUU	AGGAUGCG
10	5777	GCGCAUCC	CUGAUGA	Х	GAA	AAAUACAU	AUGUAUUUA	GGAUGCGC
	5788	CUGAAGAG	CUGAUGA	Х	GAA	AGGCGCAU	AUGCGCCUA	CUCUUCAG
	5791	ACCCUGAA	CUGAUGA	Х	GAA	AGUAGGCG	CGCCUACUC	UUCAGGGU
	5 7 93	AGACCCUG	CUGAUGA	х	GAA	AGAGUAGG	CCUACUCUU	CAGGGUCU
	5794	UAGACCCU	CUGAUGA	X	GAA	AAGAGUA G	CUACUCUUC	AGGGUCUA
15	5800	GAUCUUUA	CUGAUGA	X	GAA	ACCCUGAA	UUCAGGGUC	UAAAGAUC
	5802	UUGAUCUU	CUGAUGA	Х	GAA	AGACCCUG	CAGGGUCUA	AAGAUCAA
	5808	GCCCACUU	CUGAUGA	Х	GAA	AUCUUUAG	CUAAAGAUC	AAGUGGGC
	5819	AGCGAUCC	CUGAUGA	X	GAA	AGGCCCAC	GUGGGCCUU	GGAUCGCU
	5824	AGCUUAGC	CUGAUGA	X	GAA	AUCCAAGG	CCUUGGAUC	GCUAAGCU
20	5828	AGCCAGCU	CUGAUGA	Х	GAA	AGCGAUCC	GGAUCGCUA	AGCUGGCU
	5837	AUCAAACA	CUGAUGA	х	GAA	AGCCAGCU	AGCUGGCUC	UGUUUGAU
	5841	UAGCAUCA	CUGAUGA	X	GAA	ACAGAGCC	GGCUCUGUU	UGAUGCUA
	5842	AUAGCAUC	CUGAUGA	X	GAA	AACAGAGC	GCUCUGUUU	GAUGCUAU
	5849	UGCAUAAA	CUGAUGA	X	GAA	AGCAUCAA	UUGAUGCUA	UUUAUGCA
25	5851	CUUGCAUA	CUGAUGA	X	GAA	AUAGCAUC	GAUGCUAUU	UAUGCAAG
	5852	ACUUGCAU	CUGAUGA	X	GAA	AAUAGCAU	AUGCUAUUU	AUGCAAGU
	5853	AACUUGCA	CUGAUGA	Х	GAA	AAAUAGCA	UGCUAUUUA	UGCAAGUU
	5861	UAGACCCU	CUGAUGA	X	GAA	ACUUGCAU	AUGCAAGUU	AGGGUCUA
	5862	AUAGACCC	CUGAUGA	X	GAA	AACUUGCA	UGCAAGUUA	GGGUCUAU
30	5867	AAUACAUA	CUGAUGA	Х	GAA	ACCCUAAC	GUUAGGGUC	UAUGUAUU
	5869	UAAAUACA	CUGAUGA	X	GAA	AGACCCUA	UAGGGUCUA	UGUAUUUA
	5873	AUCCUAAA	CUGAUGA	X	GAÀ	ACAUAGAC	GUCU A UGUA	UUUAGGAU
	5875	ACAUCCUA	CUGAUGA	Х	GAA	AUACAUAG	CUAUGUAUU	UAGGAUGU

	5876	GACAUCCI	J CUGAUGA	A 2	K GAZ	A AAUACAUA	UAUGUAUUU AGGAUGUC
	5877	AGACAUC	CUGAUGA	. 2	K GA	AAAUACAU	AUGUAUUUA GGAUGUCU
	5884	AAGGUGCA	CUGAUGA		GA/	A ACAUCCUA	UAGGAUGUC UGCACCUU
	5892	GGCUGCAC	CUGAUGA	. >	(GA	AGGUGCAG	CUGCACCUU CUGCAGCC
5	5893	UGGCUGCA	CUGAUGA	. >	GA.	AAGGUGCA	UGCACCUUC UGCAGCCA
	5904	CAGCUUCU	J CUGAUGA	Σ	GAA	ACUGGCUG	CAGCCAGUC AGAAGCUG
	5930	GAAGCAGC	CUGAUGA	. Х	GAA	AUCCACUG	CAGUGGAUU GCUGCUUC
	5937	UCCCCAAG	CUGAUGA	. Х	GAA	AGCAGCAA	UUGCUGCUU CUUGGGGA
	5938	CUCCCCAA	CUGAUGA	. X	GAA	AAGCAGCA	UGCUGCUUC UUGGGGAG
10	5940	uncncccc	CUGAUGA	X	GAA	AGAAGCAG	CUGCUUCUU GGGGAGAA
	595 3	AGGAAGCA	. CUGAUGA	Х	GAA	ACUCUUCU	AGAAGAGUA UGCUUCCU
	59 58	AUAAAAGG	CUGAUGA	X	GAA	AGCAUACU	AGUAUGCUU CCUUUUAU
	5959	GAUAAAAG	CUGAUGA	X	GAA	AAGCAUAC	GUAUGCUUC CUUUUAUC
	5962	AUGGAUAA	CUGAUGA	X	GAA	AGGAAGCA	UGCUUCCUU UUAUCCAU
15	5963	CAUGGAUA	CUGAUGA	Х	GAA	AAGGAAGC	GCUUCCUUU UAUCCAUG
	5964	ACAUGGAU	CUGAUGA	X	GAA	AAAGGAAG	CUUCCUUUU AUCCAUGU
	596 5	UACAUGGA	CUGAUGA	X	GAA	AAAAGGAA	UUCCUUUUA UCCAUGUA
	5967	AUUACAUG	CUGAUGA	X	GAA	AUAAAAGG	CCUUUUAUC CAUGUAAU
	597 3	AGUUAAAU	CUGAUGA	Х	GAA	ACAUGGAU	AUCCAUGUA AUUUAACU
20	59 76	UACAGUUA	CUGAUGA	Х	GAA	AUUACAUG	CAUGUAAUU UAACUGUA
	5977	CUACAGUU	CUGAUGA	X	GAA	AAUUACAU	AUGUAAUUU AACUGUAG
	5978	UCUACAGU	CUGAUGA	X	GAA	AAAUUACA	UGUAAUUUA ACUGUAGA
	5984	UCAGGUUC	CUGAUGA	X	GAA	ACAGUUAA	UUAACUGUA GAACCUGA
	5996	GUUACUUA	CUGAUGA	Х	GAA	AGCUCAGG	CCUGAGCUC UAAGUAAC
25	5998	CGGUUACU	CUGAUGA	X	GAA	AGAGCUCA	UGAGCUCUA AGUAACCG
	6002	UCUUCGGU	CUGAUGA	X	GAA	ACUUAGAG	CUCUAAGUA ACCGAAGA
	6015	CAGAGGCA	CUGAUGA	X	GAA	ACAUUCUU	AAGAAUGUA UGCCUCUG
	6021	UAAGAACA	CUGAUGA	X	GAA	AGGCAUAC	GUAUGCCUC UGUUCUUA
	6025	CACAUAAG	CUGAUGA	X	GAA	ACAGAGGC	GCCUCUGUU CUUAUGUG
30	6026	GCACAUAA	CUGAUGA	X	GAA	AACAGAGG	CCUCUGUUC UUAUGUGC
	6028	UGGCACAU	CUGAUGA	Х	GAA	AGAACAGA	UCUGUUCUU AUGUGCCA
	6029	GUGGCACA	CUGAUGA	X	GAA	AAGAACAG	CUGUUCUUA UGUGCCAC
	6040	UAAACAAG	CUGAUGA	X	GAA	AUGUGGCA	UGCCACAUC CUUGUUUA

	6043	CUUUAAAC	CUGAUGA	X	GAA	AGGAUGUG	CACAUCCUU	GUUUAAAG
	6046	AGCCUUUA	CUGAUGA	X	GAA	ACAAGGAU	AUCCUUGUU	UAAAGGCU
	6047	GAGCCUUU	CUGAUGA	X	GAA	AACAAGGA	uccuuguuu	AAAGGCUC
	6048	AGAGCCUU	CUGAUGA	X	GAA	AAACAAGG	CCUUGUUUA	AAGGCUCU
5	6055	CAUACAGA	CUGAUGA	X	GAA	AGCCUUUA	UAAAGGCUC	UCUGUAUG
	6057	UUCAUACA	CUGAUGA	Х	GAA	AGAGCCUU	AAGGCUCUC	UGUAUGAA
	6061	UCUCUUCA	CUGAUGA	Х	GAA	ACAGAGAG	CUCUCUGUA	UGAAGAGA
	6079	GUGCUGAU	CUGAUGA	Х	GAA	ACGGUCCC	GGGACCGUC	AUCAGCAC
	6082	AAUGUGCU	CUGAUGA	X	GAA	AUGACGGU	ACCGUCAUC	AGCACAUU
10	6090	CACUAGGG	CUGAUGA	Х	GAA	AUGUGCUG	CAGCACAUU	CCCUAGUG
	6091	UCACUAGG	CUGAUGA	Х	GAA	AAUGUGCU	AGCACAUUC	CCUAGUGA
	6095	AGGCUCAC	CUGAUGA	Х	GAA	AGGGAAUG	CAUUCCCUA	GUGAGCCU
	6104	GGAGCCAG	CUGAUGA	X	GAA	AGGCUCAC	GUGAGCCUA	CUGGCUCC
	6111	GCUGCCAG	CUGAUGA	X	GAA	AGCCAGUA	UACUGGCUC	CUGGCAGC
15	6124	UUCCACAA	CUGAUGA	X	GAA	AGCCGCUG	CAGCGGCUU	UUGUGGAA
	6125	CUUCCACA	CUGAUGA	Х	GAA	AAGCCGCU	AGCGGCUUU	UGUGGAAG
	6126	UCUUCCAC	CUGAUGA	Х	GAA	AAAGCCGC	GCGGCUUUU	GUGGAAGA
	6137	UGGCUAGU	CUGAUGA	X	GAA	AGUCUUCC	GGAAGACUC	ACUAGCCA
	6141	CUUCUGGC	CUGAUGA	X	GAA	AGUGAGUC	GACUCACUA	GCCAGAAG
20	6166	GUGGAGAG	CUGAUGA	Х	GAA	ACUGUCCC	GGGACAGUC	CUCUCCAC
	6169	UUGGUGGA	CUGAUGA	X	GAA	AGGACUGU	ACAGUCCUC	UCCACCAA
	6171	UCUUGGUG	CUGAUGA	Х	GAA	AGAGGACU	AGUCCUCUC	CACCAAGA
	6181	UGGAUUUA	CUGAUGA	X	GAA	AUCUUGGU	ACCAAGAUC	UAAAUCCA
	6183	UUUGGAUU	CUGAUGA	Х	GAA	AGAUCUUG	CAAGAUCUA	AAUCCAAA
25	6187	UUUGUUUG	CUGAUGA	Х	GAA	AUUUAGAU	AUCUAAAUC	CAAACAAA
	6204	UCUGGCUC	CUGAUGA	Х	GAA	AGCCUGCU	AGCAGGCUA	GAGCCAGA
	6226	ACAACAAA	CUGAUGA	Х	GAA	AUUUGUCC	GGACAAAUC	UUUGUUGU
	6228	GAACAACA	CUGAUGA	X	GAA	AGAUUUGU	ACAAAUCUU	UGUUGUUC
	6229	GGAACAAC	CUGAUGA	X	GAA	AAGAUUUG	CAAAUCUUU	GUUGUÜCC
30	6232	AGAGGAAC	CUGAUGA	Х	GAA	ACAAAGAU	AUCUUUGUU	GUUCCUCU
	6235	AGAAGAGG	CUGAUGA	X	GAA	ACAACAAA	บบบดบบดบบ	ccucuucu
	6236	AAGAAGAG	CUGAUGA	X	GAA	AACAACAA	UUGUUGUUC	cucuucuu
	6239	GUAAAGAA	CUGAUGA	Х	GAA	AGGAACAA	UUGUUCCUC	UUCUUUAC

	6241	GUGUAAAG	CUGAUGA	. x	GAA	AGAGGAAC	GUUCCUCU	CUUUACAC
	6242	UGUGUAAA	CUGAUGA	. x	GAA	AAGAGGAA	บบดดบดบบด	UUUACACA
	6244	UAUGUGUA	CUGAUGA	X	GAA	AGAAGAGG	ccucuucuu	UACACAUA
	6245	GUAUGUGU	CUGAUGA	X	GAA	AAGAAGAG	cucuucuuu	ACACAUAC
5	6246	CGUAUGUG	CUGAUGA	X	GAA	AAAGAAGA	UCUUCUUUA	CACAUACG
	6252	GGUUUGCG	CUGAUGA	X	GAA	AUGUGUAA	UUACACAUA	CGCAAACC
	6280	AUUUUAUAA	CUGAUGA	X	GAA	AUUGCCAG	CUGGCAAUU	UUAAAAU
	6281	GAUUUAUA	CUGAUGA	Х	GAA	AAUUGCCA	UGGCAAUUU	UAUAAAUC
	6282	UGAUUUAU	CUGAUGA	Х	GAA	AAAUUGCC	GGCAAUUUU	AUAAAUCA
10	6283	CUGAUUUA	CUGAUGA	Х	GAA	AAAAUUGC	GCAAUUUUA	UAAAUCAG
	6285	ACCUGAUU	CUGAUGA	Х	GAA	AUAAAAUU	AUAUUUUAA	AAUCAGGU
	6289	AGUUACCU	CUGAUGA	X	GAA	AAUAUUA	UUAUAAAUC	AGGUAACU
	6294	CUUCCAGU	CUGAUGA	Х	GAA	ACCUGAUU	AAUCAGGUA	ACUGGAAG
	6308	CUGAGUUU	CUGAUGA	Х	GAA	ACCUCCUU	AAGGAGGUU	AAACUCAG
15	6309	UCUGAGUU	CUGAUGA	X	GAA	AACCUCCU	AGGAGGUUA	AACUCAGA
	6314	ບບບບບບ	CUGAUGA	X	GAA	AGUUUAAC	GUUAAACUC	AGAAAAA
	6331	AAUUGACU	CUGAUGA	Х	GAA	AGGUCUUC	GAAGACCUC	AGUCAAUU
	6335	AGAGAAUU	CUGAUGA	х	GAA	ACUGAGGU	ACCUCAGUC	AAUUCUCU
	6339	AAGUAGAG	CUGAUGA	Х	GAA	AUUGACUG	CAGUCAAUU	CUCUACUU
20	634 0	AAAGUAGA	CUGAUGA	X	GAA	AAUUGACU	AGUCAAU UC	UCUACUUU
	6342	AAAAAGUA	CUGAUGA	Х	GAA	AGAAUUGA	UCAAUUCUC	UACUUUUU
	6344	AAAAAAAG	CUGAUGA	х	GAA	AGAGAAUU	AAUUCUCUA	CUUUUUUU
	6347	AAAAAAA	CUGAUGA	X	GAA	AGUAGAGA	UCUCUACUU	บบบบบบบบ
	6348	AAAAAAA	CUGAUGA	X	GAA	AAGUAGAG	CUCUACUUU	บบบบบบบบ
25	6349	AAAAAAA	CUGAUGA	X	GAA	AAAGUAGA	UCUACUUUU	עעעעעעעעע
	6350	AAAAAAA	CUGAUGA	X	GAA	AAAAGUAG	CUACUUUUU	บบบบบบบบ
	6351	AAAAAAA	CUGAUGA	х	GAA	AAAAAGUA	UACUUUUUU	บบบบบบบบ
	6352	AAAAAAA	CUGAUGA	x	GAA	AAAAAAGU	ACUUUUUUU	บบบบบบบบ
	6353	AAAAAAA	CUGAUGA	x	GAA	AAAAAAAG	cuuuuuuu	עעעעעעעעע
30	6354	GAAAAAA	CUGAUGA	Х	GAA	AAAAAAA	ບບບບບບບບ	บบบบบบบ
	6355	GGAAAAA	CUGAUGA	X	GAA	AAAAAAA	ບບບບບບບບ	บบบบบบ
	6356	UGGAAAAA	CUGAUGA	х	GAA	AAAAAAA	ບບບບບບບບ	UUUUUCCA
	6357	UUGGAAAA	CUGAUGA	X	GAA	AAAAAAA	ບບບບບບບບ	UUUUCCAA

	6358	UUUGGAAA	CUGAUGA	X	GAA	AAAAAA	บบบบบบบบบ	UUUCCAAA
	6359	AUUUGGAA	CUGAUGA	Х	GAA	AAAAAA	บบบบบบบบบบ	UUCCAAAU
	6360	GAUUUGGA	CUGAUGA	х	GAA	AAAAAA	บบบบบบบบบบบบบบบบบบบบบบบบบบบบบบบบบบบบบบบ	UCCAAAUC
	6361	UGAUUUGG	CUGAUGA	x	GAA	AAAAAA	บบบบบบบบบ	CCAAAUCA
5	6362	CUGAUUUG	CUGAUGA	X	GAA	AAAAAA	שטטטטטטטכ	CAAAUCAG
	6368	UAUUAUCU	CUGAUGA	X	GAA	AUUUGGAA	UUCCAAAUC	AGAUAAUA
	637 3	UGGGCUAU	CUGAUGA	X	GAA	AUCUGAUU	AAUCAGAUA	AUAGCCCA
	6376	UGCUGGGC	CUGAUGA	Х	GAA	AUUAUCUG	CAGAUAAUA	GCCCAGCA
	6388	GUUAUCAC	CUGAUGA	Х	GAA	AUUUGCUG	CAGCAAAUA	GUGAUAAC
10	6394	UUAUUUGU	CUGAUGA	Х	GAA	AUCACUAU	AUAGUGAUA	ACAAAUAA
	6401	UAAGGUUU	CUGAUGA	Х	GAA	AUUUGUUA	UAACAAAUA	AAACCUUA
	6408	GAACAGCU	CUGAUGA	х	GAA	AGGUUUUA	UAAAACCUU	AGCUGUUC
	6409	UGAACAGC	CUGAUGA	х	GAA	AAGGUUUU	AAAACCUUA	GCUGUUCA
	6415	AAGACAUG	CUGAUGA	х	GAA	ACAGCUAA	UUAGCUGUU	CAUGUCUU
15	6416	CAAGACAU	CUGAUGA	X	GAA	AACAGCUA	UAGCUGUUC	AUGUCUUG
	6421	GAAAUCAA	CUGAUGA	X	GAA	ACAUGAAC	GUUCAUGUC	UUGAUUUC
	6423	UUGAAAUC	CUGAUGA	X	GAA	AGACAUGA	UCAUGUCUU	GAUUUCAA
	6427	AUUAUUGA	CUGAUGA	х	GAA	AUCAAGAC	GUCUUGAUU	UCAAUAAU
	6428	AAUUAUUG	CUGAUGA	X	GAA	AAUC AAG A	UCUUGAUUU	CAAUAAUU
20	6429	UUAUUAUU	CUGAUGA	Х	GAA	AAAUC AA G	CUUGAUUUC	AUUAAUUA
	6433	GAAUUAAU	CUGAUGA	X	GAA	AUUGAAAU	AUUUCAAUA	AUUAAUUC
	6436	UAAGAAUU	CUGAUGA	Х	GAA	AUUAUUGA	UCAAUAAUU	AAUUCUUA
	6437	UUAAGAAU	CUGAUGA	Х	GAA	AAUUAUUG	CAAUAAUUA	AUUCUUAA
	644 0	UGAUUAAG	CUGAUGA	Х	GAA	AUUAAUUA	UUAAUUAAUU	CUUAAUCA
25	6441	AUGAUUAA	CUGAUGA	X	GAA	UUAAUUAA	AAUUAAUUC	UUAAUCAU
	6443	UAAUGAUU	CUGAUGA	X	GAA	AGAAUUAA	UUAAUUCUU	AAUCAUUA
	6444	UUAAUGAU	CUGAUGA	Х	GAA	AAGAAUUA	UAAUUCUUA	AUCAUUAA
	6447	CUCUUAAU	CUGAUGA	Х	GAA	AUUAAGAA	UUCUUAAUC	AUUAAGAG
	6450	GGUCUCUU	CUGAUGA	X	GAA	AUGAUUAA	UUAAUCAUU	AAGAGACC
30	6451	UGGUCUCU	CUGAUGA	X	GAA	AAUG A UUA	UAAUCAUUA	AGAGACCA
	6461	GUAUUUAU	CUGAUGA	X	GAA	AUGGUCUC	GAGACCAUA	AUAAAUAC
. ,	6464	GGAGUAUU	CUGAUGA	X	GAA	AUUAUGGU	ACCAUAAUA	AAUACUCC
	6468	AAAAGGAG	CUGAUGA	Х	GAA	AUUAUUUA	UAAUAAAUA	cuccuuuu

	04/1	OUGAAAA	G CUGAUG	4 1	X GAA	A AGUAUUUA	UAAAUACU(CUUUUCA
	6474	CUCUUGA	A CUGAUGA	A 2	K GA	A AGGAGUAU	AUACUCCUT	J UUCAAGA
	6475	UCUCUUG	A CUGAUG!	A 2	K GAA	A AAGGAGUA	UACUCCUU	J UCAAGAGA
	6476	บบดบดบบ	G CUGAUGA	A)	(GA	AAAGGAGU	ACUCCUUU	J CAAGAGA
5	6477	υυυςυςυτ	J CUGAUGA	A >	(GA	AAAAGGAG	CUCCUUUUC	AAGAGAA
	6497	ACAAUUCI	J CUGAUGA	Α .	GA,	AUGGUUUU	AAAACCAUU	J AGAAUUGU
	6498	AACAAUU	C CUGAUGA	X	GA.	AAUGGUUU	AAACCAUUA	GAAUUGUU
	65 03	UGAGUAA	CUGAUGA	X	GAA	AUUCUAAU	AUUAGAAUU	GUUACUCA
	6506	AGCUGAGU	J CUGAUGA	X	GAA	ACAAUUCU	AGAAUUGUU	ACUCAGCU
10	6507	GAGCUGAG	CUGAUGA	X	GAA	AACAAUUC	GAAUUGUUA	CUCAGCUC
	6510	AAGGAGCU	J CUGAUGA	. x	GAA	AGUAACAA	UUGUUACUC	AGCUCCUU
	6 5 15	GUUUGAAG	CUGAUGA	. x	GAA	AGCUGAGU	ACUCAGCUC	CUUCAAAC
	6518	UGAGUUUG	CUGAUGA	X	GAA	AGGAGCUG	CAGCUCCUU	CAAACUCA
	6519	CUGAGUUU	CUGAUGA	X	GAA	AAGGAGCU	AGCUCCUUC	AAACUCAG
15	652 5	ACAAACCU	CUGAUGA	Х	GAA	AGUUUGAA	UUCAAACUC	AGGUUUGU
	6530	AUGCUACA	CUGAUGA	X	GAA	ACCUGAGU	ACUCAGGUU	UGUAGCAU
	6531	UAUGCUAC	CUGAUGA	Х	GAA	AACCUGAG	CUCAGGUUU	GUAGCAUA
	6534	AUGUAUGC	CUGAUGA	X	GAA	ACAAACCU	AGGUUUGUA	GCAUACAU
	653 9	GACUCAUG	CUGAUGA	X	GAA	AUGCUACA	UGUAGCAUA	CAUGAGUC
20	6547	GAUGGAUG	CUGAUGA	Х	GAA	ACUCAUGU	ACAUGAGUC	CAUCCAUC
	6551	GACUGAUG	CUGAUGA	Х	GAA	AUGGACUC	GAGUCCAUC	CAUCAGUC
	655 5	CUUUGACU	CUGAUGA	X	GAA	AUGGAUGG	CCAUCCAUC	AGUCAAAG
	65 59	CAUUCUUU	CUGAUGA	Х	GAA	ACUGAUGG	CCAUCAGUC	AAAGAAUG
	6570	CCAGAUGG	CUGAUGA	Х	GAA	ACCAUUCU	AGAAUGGUU	CCAUCUGG
25	6571	UCCAGAUG	CUGAUGA	Х	GAA	AACCAUUC	GAAUGGUUC	CAUCUGGA
	657 5	AGACUCCA	CUGAUGA	X	GAA	AUGGAACC	GGUUCCAUC	UGGAGUCU
	6582	UACAUUAA	CUGAUGA	X	GAA	ACUCCAGA	UCUGGAGUC	UUAAUGUA
	6584	UCUACAUU	CUGAUGA	X	GAA	AGACUCCA	UGGAGUCUU	AAUGUAGA
	658 5	UUCUACAU	CUGAUGA	Х	GAA	AAGACUCC	GGAGUCUUA	AUGUAGAA
0	6590	חחחכחחחכ	CUGAUGA	Х	GAA	ACAUUAAG	CUUAAUGUA	GAAAGAAA
	6609					AGUCUCCA		GUAAUAAU
	6612	CUCAUUAU	CUGAUGA	Х	GAA	ACAAGUCU	AGACUUGUA	AUAAUGAG
	6615	UAGCUCAU	CUGAUGA	Х	GAA	AUUACAAG	CUUGUAAUA	AUGAGCUA

	0023	UUUGUAAC	CUGAUGA	Х	GAA	AGCUCAUU	AAUGAGCUA	GUUACAAA
	6626	CACUUUGU	CUGAUGA	X	GAA	ACUAGCUC	GAGCUAGUU	ACAAAGUG
	6627	GCACUUUG	CUGAUGA	X	GAA	AACUAGCU	AGCUAGUUA	CAAAGUGC
	6637	UAAUGAAC	CUGAUGA	X	GAA	AGCACUUU	AAAGUGCUU	GUUCAUUA
5	6640	UUUUAAUG	CUGAUGA	x	GAA	ACAAGCAC	GUGCUUGUU	CAUUAAAA
	6641	UAAUUUUA	CUGAUGA	X	GAA	AACAAGCA	UGCUUGUUC	AUUAAAAU
	6644	GCUAUUUU	CUGAUGA	x	GAA	AUGAACAA	UUGUUCAUU	AAAAUAGC
	6645	UGCUAUUU	CUGAUGA	x	GAA	AAUGAACA	UGUUCAUUA	AAAUAGCA
	6650	UUCAGUGC	CUGAUGA	Х	GAA	UAAUUUUA	AUUAAAAUA	GCACUGAA
10	6662	CAUGUUUC	CUGAUGA	х	GAA	AUUUUCAG	CUGAAAAUU	GAAACAUG
	6674	UAUCAGUU	CUGAUGA	Х	GAA	AUUCAUGU	ACAUGAAUU	AACUGAUA
	66 75	UUAUCAGU	CUGAUGA	X	GAA	AAUUCAUG	CAUGAAUUA	ACUGAUAA
	6682	UGGAAUAU	CUGAUGA	х	GAA	AUCAGUUA	UAACUGAUA	AUAUUCCA
	6685	GAUUGGAA	CUGAUGA	Х	GAA	AUUAUCAG	CUGAUAAUA	UUCCAAUC
15	6687	AUGAUUGG	CUGAUGA	x	GAA	AUAUUAUC	GAUAAUAUU	CCAAUCAU
	6 68 8	AAUGAUUG	CUGAUGA	х	GAA	UAUUAU	AUAAUAUUC	CAAUCAUU
	669 3	UGGCAAAU	CUGAUGA	х	GAA	AUUGGAAU	AUUCCAAUC	AUUUGCCA
	6696	AAAUGGCA	CUGAUGA	x	GAA	AUGAUUGG	CCAAUCAUU	UGCCAUUU
	6697	UAAAUGGC	CUGAUGA	X	GAA	AAUGAUUG	CAAUCAUUU	GCCAUUUA
20	6703	UUGUCAUA	CUGAUGA	x	GAA	AUGGCAAA	UUUGCCAUU	UAUGAC A A
	6704	UUUGUCAU	CUGAUGA	х	GAA	AAUGGCAA	UUGCCAUUU	AUGACAAA
	6705	UUUUGUCA	CUGAUGA	X	GAA	AAAUGGCA	UGCCAUUUA	UGACA AA A
	6719	UUAGUGCC	CUGAUGA	X	GAA	ACCAUUUU	AAAAUGGUU	GGCACU A A
	6726	UUCUUUGU	CUGAUGA	х	GAA	AGUGCCAA	UUGGCACUA	ACAAAGAA
25	6743	CUGAAAGG	CUGAUGA	X	GAA	AGUGCUCG	CGAGCACUU	CCUUUCAG
	6744	UCUGAAAG	CUGAUGA	Х	GAA	AAGUGCUC	GAGCACUUC	CUUUCAGA
	6747	AACUCUGA	CUGAUGA	X	GAA	AGGAAGUG	CACUUCCUU	UCAGAGUU
	6748	AAACUCUG	CUGAUGA	Х	GAA	AAGGAAGU	ACUUCCUUU	CAGAGUUU
	6749	GAAACUCU	CUGAUGA	Х	GAA	AAAGGAAG	CUUCCUUUC	AGAGUUUC
30	6755	AUCUCAGA	CUGAUGA	X	GAA	ACUCUGAA	UUCAGAGUU	UCUGAGAU
	6756	UAUCUCAG	CUGAUGA	Х	GAA	AACUCUGA	UCAGAGUUU	CUGAGAUA
	6757	UUAUCUCA	CUGAUGA	X	GAA	AAACUCUG	CAGAGUUUC	UGAGAUAA
	6764	ACGUACAU	CUGAUGA	Х	GAA	AUCUCAGA	UCUGAGAUA	AUGUACGU

	6769	GUUCCAC	G CUGAUGA	X	GAA	ACAUUAUC	GAUAAUGUA CGUGGAAC
	6781	UCCACCCA	A CUGAUGA	Х	GAA	ACUGUUCC	GGAACAGUC UGGGUGGA
	6814	AAGACACA	CUGAUGA	X	GAA	ACUUGCAC	GUGCAAGUC UGUGUCUU
	6820	ACUGACAA	CUGAUGA	X	GAA	ACACAGAC	GUCUGUGUC UUGUCAGU
5	6822	GGACUGAC	CUGAUGA	x	GAA	AGACACAG	CUGUGUCUU GUCAGUCC
	6825	CUUGGACU	CUGAUGA	X	GAA	ACAAGACA	UGUCUUGUC AGUCCAAG
	6829	ACUUCUUG	CUGAUGA	X	GAA	ACUGACAA	UUGUCAGUC CAAGAAGU
	6851	CUAAAAUU	CUGAUGA	X	GAA	ACAUCUCG	CGAGAUGUU AAUUUUAG
	6852	CCUAAAAU	CUGAUGA	X	GAA	AACAUCUC	GAGAUGUUA AUUUUAGG
10	6855	GUCCCUAA	. CUGAUGA	X	GAA	AUUAACAU	AUGUUAAUU UUAGGGAC
	6856	GGUCCCUA	CUGAUGA	X	GAA	AAUUAACA	UGUUAAUUU UAGGGACC
	6857	GGGUCCCU	CUGAUGA	x	GAA	AAAUUAAC	GUUAAUUUU AGGGACCC
	6858	CGGGUCCC	CUGAUGA	х	GAA	AAAAUUAA	UUAAUUUUA GGGACCCG
	6872	UAGGAAAC	CUGAUGA	x	GAA	AGGCACGG	CCGUGCCUU GUUUCCUA
15	6875	GGCUAGGA	CUGAUGA	Х	GAA	ACAAGGCA	UGCCUUGUU UCCUAGCC
	68 76	GGGCUAGG	CUGAUGA	Х	GAA	AACAAGGC	GCCUUGUUU CCUAGCCC
	6877	UGGGCUAG	CUGAUGA	X	GAA	AAACAAGG	CCUUGUUUC CUAGCCCA
	6880	UUGUGGGC	CUGAUGA	Х	GAA	AGGAAACA	UGUUUCCUA GCCCACAA
	6901	AUCUGUUU	CUGAUGA	Х	GAA	AUGUUUGC	GCAAACAUC AAACAGAU
20	6910	CUAGCGAG	CUGAUGA	Х	GAA	AUCUGUUU	AAACAGAUA CUCGCUAG
	6913	AGGCUAGC	CUGAUGA	х	GAA	AGUAUCUG	CAGAUACUC GCUAGCCU
	6917	AAUGAGGC	CUGAUGA	X	GAA	AGCGAGUA	UACUCGCUA GCCUCAUU
	6922	UAAAUUUA	CUGAUGA	х	GAA	AGGCUAGC	GCUAGCCUC AUUUAAAU
	6925	UCAAUUUA	CUGAUGA	x	GAA	AUGAGGCU	AGCCUCAUU UAAAUUGA
25	6926	AUCAAUUU	CUGAUGA	х	GAA	AAUGAGGC	GCCUCAUUU AAAUUGAU
	6927	AAUCAAUU	CUGAUGA	Х	GAA	AAAUGAGG	CCUCAUUUA AAUUGAUU
	6931	CUUUAAUC	CUGAUGA	Х	GAA	UAAAUUUA	AUUUAAAUU GAUUAAAG
	6935	ccuccuuu	CUGAUGA	Х	GAA	AUCAAUUU	AAAUUGAUU AAAGGAGG
	6936	UCCUCCUU	CUGAUGA	х	GAA	AAUCAAUU	AAUUGAUUA AAGGAGGA
30	6951	CGGCCAAA	CUGAUGA	X	GAA	AUGCACUC	GAGUGCAUC UUUGGCCG
	6953	GUCGGCCA	CUGAUGA	X	GAA	AGAUGCAC	GUGCAUCUU UGGCCGAC
	6954	UGUCGGCC	CUGAUGA	Х	GAA	AAGAUGCA	UGCAUCUUU GGCCGACA
	6970	CACACAGU	CUGAUGA	X	GAA	ACACCACU	AGUGGUGUA ACUGUGUG

	7026	AACACACA	CUGAUGA	Х	GAA	ACACCCAC	GUGGGUGUA	UGUGUGUU
	7034	AUGCACAA	CUGAUGA	Х	GAA	ACACACAU	AUGUGUGUU	UUGUGCAU
	7035	UAUGCACA	CUGAUGA	Х	GAA	AACACACA	UGUGUGUUU	UGUGCAUA
	7036	UUAUGCAC	CUGAUGA	Х	GAA	AAACACAC	GUGUGUUUU	GUGCAUAA
5	7043	UAAAUAGU	CUGAUGA	x	GAA	AUGCACAA	UUGUGCAUA	ACUAUUUA
	7047	UCCUUAAA	CUGAUGA	X	GAA	AGUUAUGC	GCAUAACUA	UUUAAGGA
	7049	UUUCCUUA	CUGAUGA	Х	GAA	AUAGUUAU	AUAACUAUU	UAAGGAAA
	7050	GUUUCCUU	CUGAUGA	х	GAA	AAUAGUUA	UAACUAUUU	AAGGAAAC
	7051	AGUUUCCU	CUGAUGA	х	GAA	AAAUAGUU	AACUAUUUA	AGGAAACU
10	7065	AACUUUAA	CUGAUGA	Х	GAA	AUUCCAGU	ACUGGAAUU	UUAAAGUU
	7066	UAACUUUA	CUGAUGA	Х	GAA	AAUUCCAG	CUGGAAUUU	UAAAGUUA
	7 067	GUAACUUU	CUGAUGA	X	GAA	AAAUUCCA	UGGAAUUUU	AAAGUUAC
	7068	AGUAACUU	CUGAUGA	X	GAA	AAAAUUCC	GGAAUUUUA	AAGUUACU
	7073	AUAAAAGU	CUGAUGA	X	GAA	ACUUUAAA	UUUAAAGUU	ACUUUUAU
15	7074	UAUAAAAG	CUGAUGA	Х	GAA	AACUUUAA	UUAAAGUUA	CUUUUAUA
	7077	UUGUAUAA	CUGAUGA	Х	GAA	AGUAACUU	AAGUUACUU	UUAUACAA
	7078	UUUGUAUA	CUGAUGA	X	GAA	AAGUAACU	AGUUACUUU	UAUACAAA
	7079	GUUUGUAU	CUGAUGA	X	GAA	AAAGUAAC	GUUACUUUU	AUACAAAC
	7080	GGUUUGUA	CUGAUGA	X	GAA	AAAAGUAA	UUACUUUUA	UACAAACC
20	7082	UUGGUUUG	CUGAUGA	Х	GAA	AUAAAAGU	ACUUUUAUA	CAAACCAA
	7095	GUAGCAUA	CUGAUGA	Х	GAA	AUUCUUGG	CCAAGAAUA	UAUGCUAC
	7097	CUGUAGCA	CUGAUGA	Х	GAA	AUAUUCUU	AAGAAUAUA	UGCUACAG
	7102	UAUAUCUG	CUGAUGA	X	GAA	AGCAUAUA	UAUAUGCUA	CAGAUAUA
	7108	CUGUCUUA	CUGAUGA	Х	GAA	AUCUGUAG	CUACAGAUA	UAAGACAG
25	7110	GUCUGUCU	CUGAUGA	X	GAA	AUAUCUGU	ACAGAUAUA	AGACAGAC
	7124	UAGGACCA	CUGAUGA	X	GAA	ACCAUGUC	GACAUGGUU	UGGUCCUA
	7125	AUAGGACC	CUGAUGA	X	GAA	AACCAUGU	ACAUGGUUU	GGUCCUAU
	7129	AAAUAUAG	CUGAUGA	Х	GAA	ACCAAACC	GGUUUGGUC	CUAUAUUU
	7132	UAGAAAUA	CUGAUGA	X	GAA	AGGACCAA	UUGGUCCUA	UAUUUCUA
30	7134	ACUAGAAA	CUGAUGA	X	GAA	AUAGGACC	GGUCCUAUA	UUUCUAGU
	7136	UGACUAGA	CUGAUGA	Х	GAA	AUAUAGGA	UCCUAUAUU	UCUAGUCA
	7137	AUGACUAG	CUGAUGA	Х	GAA	AAUAUAGG	CCUAUAUUU	CUAGUCAU
	7138	CAUGACUA	CUGAUGA	X	GAA	AAAUAUAG	CUAUAUUUC	UAGUCAUG

	7140	AUCAUGAC	CUGAUGA	X	GAA	AGAAAUAU	AUAUUUCUA	GUCAUGAU
	7143	UUCAUCAU	CUGAUGA	X	GAA	ACUAGAAA	UUUCUAGUC	AUGAUGAA
	7155	AUACAAAA	CUGAUGA	X	GAA	ACAUUCAU	AUGAAUGUA	UUUUGUAU
	7157	GUAUACAA	CUGAUGA	. X	GAA	AUACAUUC	GAAUGUAUU	UUGUAUAC
5	7158	GGUAUACA	CUGAUGA	. x	GAA	AAUACAUU	AAUGUAUUU	UGUAUACC
	7159	UGGUAUAC	CUGAUGA	. X	GAA	AAAUACAU	AUGUAUUUU	GUAUACCA
	7162	AGAUGGUA	CUGAUGA	. X	GAA	ACAAAAUA	UAUUUUGUA	UACCAUCU
	7164	GAAGAUGG	CUGAUGA	X	GAA	AUACAAAA	UUUUGUAUA	CCAUCUUC
	7169	UAUAUGAA	CUGAUGA	Х	GAA	AUGGUAUA	UAUACCAUC	UUCAUAUA
10	7171	AUUAUAUG	CUGAUGA	Х	GAA	AGAUGGUA	UACCAUCUU	CAUAUAAU
	71 72	UAUUAUAU	CUGAUGA	Х	GAA	AAGAUGGU	ACCAUCUUC	AUAUAAUA
	7175	GUAUAUUA	CUGAUGA	Х	GAA	AUGAAGAU	AUCUUCAUA	UAAUAUAC
	7177	AAGUAUAU	CUGAUGA	х	GAA	AUAUGAAG	CUUCAUAUA	AUAUACUU
	7180	UUUAAGUA	CUGAUGA	X	GAA	AUUAUAUG	CAUAUAAUA	UACUUAAA
15	7182	UUUUUAAG	CUGAUGA	X	GAA	AUAUUAUA	UAUAAUAUA	CUUAAAAA
	7185	UUUUUAUA	CUGAUGA	х	GAA	AGUAUAUU	AAUAUACUU	AAAAAUAU
	7186	AAUAUUUU	CUGAUGA	Х	GAA	AAGUAUAU	AUAUACUUA	UUAUAAAA
	7192	UUAAGAAA	CUGAUGA	х	GAA	AAUUUUUA	UUAAAAAUA	UUUCUUAA
	7194	AAUUAAGA	CUGAUGA	x	GAA	UUUUUAUA	UUAUAAAAA	UCUUAAUU
20	71 95	CAAUUAAG	CUGAUGA	X	GAA	AAUAUUUU	AAAAUAUUU	CUUAAUUG
	7.196	CCAAUUAA	CUGAUGA	x	GAA	UUUAUAAA	AAAUAUUUC	UUAAUUGG
	7198	UCCCAAUU	CUGAUGA	x	GAA	AGAAAUAU	AUAUUUCUU	AAUUGGGA
	719 9	AUCCCAAU	CUGAUGA	х	GAA	AAGAAAUA	UAUUUCUUA	AUUGGGAU
	7202	CAAAUCCC	CUGAUGA	x	GAA	AUUAAGAA	UUCUUAAUU	GGGAUUUG
25	7208	CGAUUACA	CUGAUGA	X	GAA	AUCCCAAU	AUUGGGAUU	UGUAAUCG
	7209	ACGAUUAC	CUGAUGA	x	GAA	AAUCCCAA	UUGGGAUUU	GUAAUCGU
	7212	GGUACGAU	CUGAUGA	x	GAA	ACAAAUCC	GGAUUUGUA	AUCGUACC
	7215	GUUGGUAC	CUGAUGA	x	GAA	AUUACAAA	UUUGUAAUC	GUACCAAC
	7218	UAAGUUGG	CUGAUGA	x	GAA	ACGAUUAC	GUAAUCGUA	CCAACUUA
30	7225	UAUCAAUU	CUGAUGA	х	GAA	AGUUGGUA	UACCAACUU	AAUUGAUA
	7226	UUAUCAAU	CUGAUGA	x	GAA	AAGUUGGU	ACCAACUUA	AUUGAUAA
	7229	AGUUUAUC	CUGAUGA	x	GAA	AUUAAGUU	AACUUAAUU	GAUAAACU
	7233	GCCAAGUU	CUGAUGA	х	GAA	AUCAAUUA	UAAUUGAUA	AACUUGGC

	/238	CAGUUGCC	CUGAUGA	Х	GAA	AGUUUAUC	GAUAAACUU	GGCAACUG
	7249	GAACAUAA	CUGAUGA	Х	GAA	AGCAGUUG	CAACUGCUU	UUAUGUUC
	7250	AGAACAUA	CUGAUGA	Х	GAA	AAGCAGUU	AACUGCUUU	UAUGUUCU
	7251	CAGAACAU	CUGAUGA	X	GAA	AAAGCAGU	ACUGCUUUU	AUGUUCUG
5	7252	ACAGAACA	CUGAUGA	Х	GAA	AAAAGCAG	CUGCUUUUA	UGUUCUGU
	7256	GGAGACAG	CUGAUGA	X	GAA	ACAUAAAA	UUUUAUGUU	CUGUCUCC
	7257	AGGAGACA	CUGAUGA	X.	GAA	AACAUAAA	UUUAUGUUC	UGUCUCCU
	7261	UGGAAGGA	CUGAUGA	X	GAA	ACAGAACA	uguucuguc	UCCUUCCA
	7263	UAUGGAAG	CUGAUGA	X	GAA	AGACAGAA	UUCUGUCUC	CUUCCAUA
10	7266	AUUUAUGG	CUGAUGA	Х	GAA	AGGAGACA	UGUCUCCUU	CCAUAAAU
	7267	AAUUUAUG	CUGAUGA	Х	GAA	AAGGAGAC	GUCUCCUUC	CAUAAAUU
	7271	GAAAAAUU	CUGAUGA	Х	GAA	AUGGAAGG	CCUUCCAUA	AAUUUUUC
	7275	UUUUGAAA	CUGAUGA	X	GAA	AUUUAUGG	CCAUAAAUU	UUUCAAAA
	7276	AUUUUGAA	CUGAUGA	Х	GAA	AAUUUAUG	CAUAAAUUU	UUCAAAAU
1 5	7277	UAUUUUGA	CUGAUGA	X	GAA	UAUUUAAA	AUAAAUUUU	UCAAAAUA
	7278	GUAUUUUG	CUGAUGA	X	GAA	AUUUAAAA	UUUUUAAAU	CAAAAUAC
	7279	AGUAUUUU	CUGAUGA	X	GAA	UUUAAAAA	AAAUUUUUC	AAAAUACU
	7285	UGAAUUAG	CUGAUGA	X	GAA	AUUUUGAA	UUCAAAAUA	CUAAUUCA
	7288	UGUUGAAU	CUGAUGA	Х	GAA	AGUAUUUU	AAAAUACUA	AUUCAACA
20	7291	CUUUGUUG	CUGAUGA	X	GAA	AUUAGUAU	AUACUAAUU	CAACAAAG
	72 92	ncnnnann	CUGAUGA	X	GAA	AAUUAGUA	UACUAAUUC	AACAAAGA
	7308	AAAAAAA	CUGAUGA	X	GAA	AGCUUUUU	AAAAAGCUC	טטטטטטטט
	7310	GGAAAAAA	CUGAUGA	X	GAA	AGAGCUUU	AAAGCUCUU	υυυυυυςς
	7311	AGGAAAAA	CUGAUGA	Х	GAA	AAGAGCUU	AAGCUCUUU	บบบบบตร
25	7312	UAGGAAAA	CUGAUGA	X	GAA	AAAGAGCU	AGCUCUUUU	UUUUCCUA
	7313	UUAGGAAA	CUGAUGA	X	GAA	AAAAGAGC	GCUCUUUUU	UUUCCUAA
	7314	UUUAGGAA	CUGAUGA	Х	GAA	AAAAGAG	CUCUUUUUU	UUCCUAAA
	7315	UUUUAGGA	CUGAUGA	X	GAA	AAAAAGA	ncnnnnnn	UCCUAAAA
	7316	AUUUUAGG	CUGAUGA	X	GAA	AAAAAAG	cuuuuuuu	CCUAAAAU
30	7317	UAUUUUAG	CUGAUGA	Х	GAA	AAAAAAA	טטטטטטטט	CUAAAAUA
	7320	GUUUAUUU	CUGAUGA	X	GAA	AGGAAAAA	UUUUUCCUA	AAAUAAAC
	7325	UUUGAGUU	CUGAUGA	Х	GAA	AUUUUAGG	CCUAAAAUA	AACUCAAA
	7330	UUUAAAUU	CUGAUGA	Х	GAA	AGUUUAUU	AAUAAACUC	AAAUUUAU

	7335	CAAGGAUA CUGAUGA X GAA AUUUGAGU	ACUCAAAUU UAUCCUUG
	7336	ACAAGGAU CUGAUGA X GAA AAUUUGAG	CUCAAAUUU AUCCUUGU
	7337	AACAAGGA CUGAUGA X GAA AAAUUUGA	UCAAAUUUA UCCUUGUU
	7339	UAAACAAG CUGAUGA X GAA AUAAAUUU	AAAUUUAUC CUUGUUUA
5	7342	CUCUAAAC CUGAUGA X GAA AGGAUAAA	UUUAUCCUU GUUUAGAG
	7345	CUGCUCUA CUGAUGA X GAA ACAAGGAU	AUCCUUGUU UAGAGCAG
	7346	UCUGCUCU CUGAUGA X GAA AACAAGGA	UCCUUGUUU AGAGCAGA
	7347	CUCUGCUC CUGAUGA X GAA AAACAAGG	CCUUGUUUA GAGCAGAG
	7362	UUUUUCUU CUGAUGA X GAA AUUUUUCU	AGAAAAAUU AAGAAAAA
10	7363	GUUUUUCU CUGAUGA X GAA AAUUUUUC	GAAAAAUUA AGAAAAAC
	73 73	CCAUUUCA CUGAUGA X GAA AGUUUUUC	GAAAAACUU UGAAAUGG
	7374	ACCAUUUC CUGAUGA X GAA AAGUUUUU	AAAAACUUU GAAAUGGU
	7383	UUUUUUGA CUGAUGA X GAA ACCAUUUC	GAAAUGGUC UCAAAAA
	7385		AAUGGUCUC AAAAAAUU
15	739 3	UAUUUAGC CUGAUGA X GAA AUUUUUUG	CAAAAAUU GCUAAAUA
	73 97	AAAAUAUU CUGAUGA X GAA AGCAAUUU	AAAUUGCUA AAUAUUUU
	7401	AUUGAAAA CUGAUGA X GAA AUUUAGCA	UGCUAAAUA UUUUCAAU
	7403	CCAUUGAA CUGAUGA X GAA AUAUUUAG	CUAAAUAUU UUCAAUGG
	7404	UCCAUUGA CUGAUGA X GAA AAUAUUUA	UAAAUAUUU UCAAUGGA
20	7405	UUCCAUUG CUGAUGA X GAA AAAUAUUU	AAAUAUUUU CAAUGGAA
	7406	UUUCCAUU CUGAUGA X GAA AAAAUAUU	AAUAUUUUC AAUGGAAA
	7418	CUAACAUU CUGAUGA X GAA AGUUUUCC	12.0000110
	7424	GCUAAACU CUGAUGA X GAA ACAUUUAG	CUAAAUGUU AGUUUAGC
2.5	7425	AGCUAAAC CUGAUGA X GAA AACAUUUA	UAAAUGUUA GUUUAGCU
25	7428	AUCAGCUA CUGAUGA X GAA ACUAACAU	AUGUUAGUU UAGCUGAU
	7429	AAUCAGCU CUGAUGA X GAA AACUAACA	UGUUAGUUU AGCUGAUU
	7430	CAAUCAGC CUGAUGA X GAA AAACUAAC	GUUAGUUUA GCUGAUUG
	7437	CCCCAUAC CUGAUGA X GAA AUCAGCUA	UAGCUGAUU GUAUGGGG
3.0		AAACCCCA CUGAUGA X GAA ACAAUCAG	CUGAUUGUA UGGGGUUU
30		GGUUCGAA CUGAUGA X GAA ACCCCAUA	UAUGGGGUU UUCGAACC
		AGGUUCGA CUGAUGA X GAA AACCCCAU	AUGGGGUUU UCGAACCU
		AAGGUUCG CUGAUGA X GAA AAACCCCA	UGGGGUUUU CGAACCUU
	7450	AAAGGUUC CUGAUGA X GAA AAAACCCC	GGGGUUUUC GAACCUUU

	7457	AAAAGUGA	CUGAUGA	X	GAA	AGGUUCGA	UCGAACCUU	UCACUUUU
	7458	AAAAAGUG	CUGAUGA	Х	GAA	AAGGUUCG	CGAACCUUU	CACUUUUU
	7459	CAAAAAGU	CUGAUGA	Х	GAA	AAAGGUUC	GAACCUUUC	ACUUUUUG
	7463	CAAACAAA	CUGAUGA	X	GAA	AGUGAAAG	CUUUCACUU	UUUGUUUG
5	7464	ACAAACAA	CUGAUGA	Х	GAA	AAGUGAAA	UUUCACUUU	UUGUUUGU
	7465	AACAAACA	CUGAUGA	X	GAA	AAAGUGAA	UUCACUUUU	UGUUUGUU
	7466	AAACAAAC	CUGAUGA	X	GAA	AAAAGUGA	UCACUUUUU	GUUUGUUU
	7469	GUAAAACA	CUGAUGA	Х	GAA	ACAAAAAG	CUUUUUGUU	UGUUUUAC
	7470	GGUAAAAC	CUGAUGA	х	GAA	AACAAAAA	บบบบบน	GUUUUACC
10	7473	AUAGGUAA	CUGAUGA	Х	GAA	ACAAACAA	undnnndnn	UUACCUAU
	7474	AAUAGGUA	CUGAUGA	X	GAA	AACAAACA	UGUUUGUUU	UACCUAUU
	7475	AAAUAGGU	CUGAUGA	X	GAA	AAACAAAC	GUUUGUUUU	ACCUAUUU
	7476	GAAAUAGG	CUGAUGA	Х	GAA	AAAACAAA	UUUGUUUUA	CCUAUUUC
	7480	UUGUGAAA	CUGAUGA	Х	GAA	AGGUAAAA	UUUUACCUA	UUUCACAA
15	7482	AGUUGUGA	CUGAUGA	X	GAA	AUAGGUAA	UUACCUAUU	UCACAACU
	7483	CAGUUGUG	CUGAUGA	X	GAA	AAUAGGUA	UACCUAUUU	CACAACUG
	7484	ACAGUUGU	CUGAUGA	Х	GAA	AAAUAGGU	ACCUAUUUC	ACAACUGU
	7495	UGGCAAUU	CUGAUGA	х	GAA	ACACAGUU	AACUGUGUA	AAUUGCCA
	7 49 9	UUAUUGGC	CUGAUGA	Х	GAA	AUUUACAC	GUGUAAAUU	GCCAAUAA
20	7506	ACAGGAAU	CUGAUGA	X	GAA	AUUGGCAA	UUGCCAAUA	AUUCCUGU
	7509	UGGACAGG	CUGAUGA	X	GAA	AUUAUUGG	CCAAUAAUU	CCUGUCCA
	7510	AUGGACAG	CUGAUGA	X	GAA	AAUUAUUG	CAAUAAUUC	CUGUCCAU
	7515	UUUUCAUG	CUGAUGA	X	GAA	ACAGGAAU	AUUCCUGUC	CAUGAAAA
	7531	CACUGGAU	CUGAUGA	X	GAA	AUUUGCAU	AUGCAAAUU	AUCCAGUG
25	7532	ACACUGGA	CUGAUGA	X	GAA	AAUUUGCA	UGCAAAUUA	UCCAGUGU
	7534	CUACACUG	CUGAUGA	Х	GAA	AUAAUUUG	CAAAUUAUC	CAGUGUAG
	7541	AAUAUAUC	CUGAUGA	X	GAA	ACACUGGA	UCCAGUGUA	GAUAUAUU
	7545	GUCAAAUA	CUGAUGA	X	GAA	AUCUACAC	GUGUAGAUA	UAUUUGAC
	7547	UGGUCAAA	CUGAUGA	Х	GAA	AUAUCUAC	GUAGAUAUA	UUUGACCA
30	7549	GAUGGUCA	CUGAUGA	X	GAA	AUAUAUCU	AGAUAUAUU	UGACCAUC
	7550	UGAUGGUC	CUGAUGA	X	GAA	AAUAUAUC	GAUAUAUUU	GACCAUCA
	75 57	CAUAGGGU	CUGAUGA	X	GAA	AUGGUCAA	UUGACCAUC	ACCCUAUG
	7563	AAUAUCCA	CUGAUGA	Х	GAA	AGGGUGAU	AUCACCCUA	UGGAUAUU

	7569	CUAGCCAA CUGAUGA X GAA AUCCAUAG	CUAUGGAUA UUGGCUAG
	7571	AACUAGCC CUGAUGA X GAA AUAUCCAU	AUGGAUAUU GGCUAGUU
	7576	GGCAAAAC CUGAUGA X GAA AGCCAAUA	UAUUGGCUA GUUUUGCC
	7579	AAAGGCAA CUGAUGA X GAA ACUAGCCA	UGGCUAGUU UUGCCUUU
5	7580	UAAAGGCA CUGAUGA X GAA AACUAGCC	GGCUAGUUU UGCCUUUA
	7581	AUAAAGGC CUGAUGA X GAA AAACUAGC	GCUAGUUUU GCCUUUAU
	7586	GCUUAAUA CUGAUGA X GAA AGGCAAAA	UUUUGCCUU UAUUAAGC
	7587	UGCUUAAU CUGAUGA X GAA AAGGCAAA	UUUGCCUUU AUUAAGCA
	7588	UUGCUUAA CUGAUGA X GAA AAAGGCAA	UUGCCUUUA UUAAGCAA
10	7590	AUUUGCUU CUGAUGA X GAA AUAAAGGC	GCCUUUAUU AAGCAAAU
	7591	AAUUUGCU CUGAUGA X GAA AAUAAAGG	CCUUUAUUA AGCAAAUU
	7599	CUGAAAUG CUGAUGA X GAA AUUUGCUU	AAGCAAAUU CAUUUCAG
	7600	GCUGAAAU CUGAUGA X GAA AAUUUGCU	AGCAAAUUC AUUUCAGC
	76 03	CAGGCUGA CUGAUGA X GAA AUGAAUUU	AAAUUCAUU UCAGCCUG
15	7604	UCAGGCUG CUGAUGA X GAA AAUGAAUU	AAUUCAUUU CAGCCUGA
	7605	UUCAGGCU CUGAUGA X GAA AAAUGAAU	AUUCAUUUC AGCCUGAA
	7617	UAUAGGCA CUGAUGA X GAA ACAUUCAG	CUGAAUGUC UGCCUAUA
	7623	AGAAUAUA CUGAUGA X GAA AGGCAGAC	GUCUGCCUA UAUAUUCU
	7625	AGAGAAUA CUGAUGA X GAA AUAGGCAG	CUGCCUAUA UAUUCUCU
20	7627	GCAGAGAA CUGAUGA X GAA AUAUAGGC	
	7629	GAGCAGAG CUGAUGA X GAA AUAUAUAG	
	7630	AGAGCAGA CUGAUGA X GAA AAUAUAUA	
	7632	AAAGAGCA CUGAUGA X GAA AGAAUAUA	UAUAUUCUC UGCUCUUU
	7637	AAUACAAA CUGAUGA X GAA AGCAGAGA	UCUCUGCUC UUUGUAUU
25	7639	AGAAUACA CUGAUGA X GAA AGAGCAGA	
	7640	GAGAAUAC CUGAUGA X GAA AAGAGCAG	CUGCUCUUU GUAUUCUC
	7643	AAGGAGAA CUGAUGA X GAA ACAAAGAG	CUCUUUGUA UUCUCCUU
	7645	CAAAGGAG CUGAUGA X GAA AUACAAAG	CUUUGUAUU CUCCUUUG
	7646	UCAAAGGA CUGAUGA X GAA AAUACAAA	UUUGUAUUC UCCUUUGA
30	7648	GUUCAAAG CUGAUGA X GAA AGAAUACA	UGUAUUCUC CUUUGAAC
	7651	CGGGUUCA CUGAUGA X GAA AGGAGAAU	AUUCUCCUU UGAACCCG
		ACGGGUUC CUGAUGA X GAA AAGGAGAA	UUCUCCUUU GAACCCGU
	7661	GAUGUUUU CUGAUGA X GAA ACGGGUUC	GAACCCGUU AAAACAUC

WO 97/15662 PCT/US96/17480

90

7662 GGAUGUUU CUGAUGA X GAA AACGGGUU AACCCGUUA AAACAUCC
7669 UGCCACAG CUGAUGA X GAA AUGUUUUA UAAAACAUC CUGUGGCA
Where "X" represents stem II region of a HH ribozyme (Hertel et al., 1992 Nucleic Acids Res. 20 3252). The length of stem II
5 may be ≥ 2 base-pairs.

	Table I	II: Human	£1 t1	VEGF Re	Table III: Human flt1 VEGF Receptor-Hairpin Ribozyme and Substrate Sequence	ance
	nt.				HP Ribozyme Sequence	Substrate
	Position	u(
	16	CGGGGAGG	AGAA	GAGAGG	CGGGGAGG AGAA GAGAGG ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	concince ech conococe
\mathcal{S}	39	ccecncce	AGAA	ລວອລວອ	CCGCUCCG AGAA GCCGCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	GGCGGCG GCU CGGAGCGG
	1.80	CCGCCAGA	AGAA	cnccnc	CCGCCAGA AGAA GUCCUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GAGGACG GAC UCUGGCGG
	190	AACGACCC	AGAA	GCCAGA	AACGACCC AGAA GCCAGA ACCAGAGAAACACGCUGUGGUACAUUACCUGGUA	nancece ecc econacenn
	278	GCGCGCAC	AGAA	GGACCC	GCGCGCAC AGAA GGACCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	aggneen gen angegeee
	290	GACAGCUG	AGAA	ລຄວຄວອ	GACAGCUG AGAA GCGCGC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	acacacu acu caacuauc
0	295	AAGCAGAC	AGAA	GAGCAG	AAGCAGAC AGAA GAGCAG ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	cuecuca ecu eucuecuu
	298	GAGAAGCA	AGAA	GCUGAG	GAGAAGCA AGAA GCUGAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	cucagcu guc ugcuncuc
	302	CUGUGAGA	AGAA	GACAGC	CUGUGAGA AGAA GACAGC ACCAGAGAAACACGCUGGUGGUACAUUACCUGGUA	GCUGUCU GCU UCUCACAG
	420	CAUUUAUG	AGAA	ccuucc	CAUTUANG AGAA GCUUCC ACCAGAGAAACACGCTUGUGGGACAUUACCUGGUA	GGAAGCA GCC CAUAAAUG
	486	CUUCCACA	AGAA	GAUUUA	CUUCCACA AGAA GAUUUA ACCAGAGAAACACGCUGGUGGUACAUUACCUGGUA	UAAAUCU GCC UGUGGAAG
Ω.	537	unuccuuc	AGAA	GUGUUC	UUUGCUUG AGAA GUGUUC ACCAGAGAAACACGCGUUGUGGUACAUUACCUGGUA	GNACACA GCU CAAGCNAA
	292	AUAUUUGC	AGAA	GUAGAA	AUAUUUGC AGAA GUAGAA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UUCUACA GCU GCAAAUAU
	721	CGUAACCC	AGAA	GGGAAU	CGUAACCC AGAA GGGAAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	AUUCCCU GCC GGGUUACG
	786	cennnncc	AGAA	GGGAUC	CGUJUUCC AGAA GGGAUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GAUCCCU GAU GGAAAACG
	863	CUUCACAG	AGAA	GAAGCC	CUUCACAG AGAA GAAGCC ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	GGCUUCU GAC CUGUGAAG

GGACCCA GAU GAAGUUCC

GGAACUUC AGAA GGGUCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

2652

	i			
	AAAGACU GAC UACCUAUC	GAUAGGUA AGAA GUCUUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	2625	
	UGGAGCU GAU CACUCUAA	UVAGAGUG AGAA GCUCCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	2525	
	CCUCACU GUU CAAGGAAC	GUUCCUUG AGAA GUGAGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	2490	
	GCACGCU GUU UAUUGAAA		2396	S
	AGCCUCA GAU CACUUGGU	ACCAAGUG AGAA GAGGCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	2321	
	AUCAGCA GUU CCACCACU	AGUGGUGG AGAA GCUGAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	2275	
	UGAAACU GUC UUGCACAG	CUGUGCAA AGAA GUUUCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	1973	
	AAAUGCC GAC GGAAGGAG	CUCCUUCC AGAA GCAUUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	1949	
	UAUCACA GAU GUGCCAAA	UUUGGCAC AGAA GUGAUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	1908	10
92	UGUGGCU GAC UCUAGAAU	AUUCUAGA AGAA GCCACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	1824	
ģ	AAAUCCU GAC UUGUACCG	CGGUACAA AGAA GGAUUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	1604	
	AGACCCG GCU CUCUACCC	GGGUAGAG AGAA GGGUCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	1572	
	GUUUCCA GAC CCGGCUCU	AGAGCCGG AGAA GGAAAC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	1566	
	AACCCCA GAU UUACGAAA	UUUCGUAA AGAA GGGGUU ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	1535	2
	GAAAUCU GCU CGCUAUUU	AAAUAGCG AGAA GAUUUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	1389	
	CUUACCG GCU CUCUAUGA	UCAUAGAG AGAA GGUAAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	1310	
	GCAAGCG GUC UVACCGGC	GCCGGUAA AGAA GCUUGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	1301	
	UVACCCU GAU GAAAAAA	UUUUUUUC AGAA GGGUAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	1056	

GCACUCU GUU GGCCUCUC

GAGAGGCC AGAA GAGUGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

							9	93	-								
GUGAGCG GCU CCCUUAUG	CGUGCCG GAC UGUGGCUG	AAGCUCU GAU GACUGAGC	UVAACCU GCU GGGAGCCU	GGCCUCU GAU GGUGAUUG	AGCUCCG GCU UUCAGGAA	GGAUUCU GAC GGUUUCUA	UCUGACG GUU UCUACAAG	AAGAUCU GAU UUCUUACA	UCUUACA GUU UUCAAGUG	AGUUCCU GUC UUCCAGAA	GAACCCC GAU UAUGUGAG	UUUUGCA GUC GCCUGAGG	UCUAUCA GAU CAUGCUGG	CUGGACU GCU GGCACAGA	AACUCCU GCC UUCUCUGA	UAUTUCA GCU CCGAAGIII	AAGCUCU GAU GAUGUCAG
CAUAAGGG AGAA GCUCAC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CAGCCACA AGAA GGCACG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GCUCAGUC AGAA GAGCUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	AGGCUCCC AGAA GGUUAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CAAUCACC AGAA GAGGCC	UUCCUGAA AGAA GGAGCU ACCAGAGAAACACGCUUGUGGUACAUUACCUGGUA	UAGAAACC AGAA GAAUCC ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CUUGUAGA AGAA GUCAGA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UGUAAGAA AGAA GAUCUU ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CACUUGAA AGAA GUAAGA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UUCUGGAA AGAA GGAACU ACCAGAGAAACACGCUUGUGGUACAUUACCUGGUA	CUCACAUA AGAA GGGUUC ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CCUCAGGC AGAA GCAAAA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CCAGCAUG AGAA GAUAGA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UCUGUGCC AGAA GUCCAG ACCAGAGAAACACGCUUGUGGUACAUUACCUGGUA	UCAGAGAA AGAA GGAGUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	AACUUCGG AGAA GAAAUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CUGACAUC AGAA GAGCUU ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA
2684	2816	2873	2930	2963	3157	3207	3211	3245	3256	3287	3402	3580	3641	3655	3810	3846	3873
				5					10					15			

AAAUGCA GUC CUGAGGAG

CUCCUCAG AGAA GCAUUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

	4100	UGACAUCA 7	AGAA	GCCCCG ACCAGAGAACA	UGACAUCA AGAA GCCCCG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	CGGGGCU GUC UGAUGUCA	
	4104	CUGCUGAC AGAA GACAGC	AGAA		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	GCUGUCU GAU GUCAGCAG	
	4120	AUGGCAGA AGAA GGGCCU	AGAA		ACCAGAGAAACACAUUGUGGUACAUUACCUGGUA	AGGCCCA GUU UCUGCCAU	•
	4135	GUGCCCAC AGAA GGAAUG	AGAA		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CAUUCCA GCU GUGGGCAC	
2	4210	GGCCGGG AGAA GCACGC	AGAA		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	acanacu acu coccacco	
	4217	AGUCUGGG AGAA GGGAGC	AGAA		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	GCUCCCC GCC CCCAGACU	
	4224	GAGUUGUA AGAA GGGGGC	AGAA		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	GCCCCCA GAC UACAACUC	
	4382	CAAAAAGC AGAA GGCUCC	AGAA		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	GGAGCCA GCU GCUUUUUG	94
	4385	UCACAAAA AGAA GCUGGC	JGAA		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	GCCAGCU GCU UUUUGUGA	
10	4537	GGGGUUGG AGAA GGGAAG	AGAA		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CUUCCCU GCU CCAACCCC	
	4573	CUCAAUCA AGAA GGUCCU	AGAA		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	AGGACCA GUU UGAUUGAG	
	4594	AUUGGGUG AGAA GUGCAG	AGAA		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CUGCACU GAU CACCCAAU	
	4628	GGCUGCAG AGAA GGCCCA	AGAA		ACCAGAGAAACACAUGUGGUACAUUACCUGGUA	UGGGCCA GCC CUGCAGCC	
	4636	GGGUUUUG AGAA GCAGGG	IGAA		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CCCUGCA GCC CAAAACCC	
15	4866	AGGGUCAG AGAA GGGAAG	IGAA		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CUUCCCA GCU CUGACCCU	
	4871	GUAGAAGG AGAA GAGCUG	\GAA		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CAGCUÇU GAC CCUUCUAC	
	4905	CGCUGUCC AGAA GCUCCU	GAA		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	AGGAGCA GAU GGACAGCG	
	5233	CUGUGCAA AGAA GAAUAA	GAA	GAAUAA ACCAGAGAAACAC	ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UVAUVCU GUV UVGCACAG	

UCCUUCCA

CNC

AUGUUCU

UGGAAGGA AGAA GAACAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

7258

7433

CCCAUACA AGAA GCUAAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

JUVAGCU GAU UGUAUGGG

GAGGGCU GAU GGAGGAAA AGACCCC GUC UCUAUACC GUU GGGACUCA UGGCUCU GUU UGAUGCUA CAACACA GUU GGGACCCA UNCAACU GCU UUGAAACU UGGCUCU GUU UGAUGCUA GAUUGCU GCU UCUUGGGG UGCCUCU GUU CUUAUGUG GCU UUUGUGGA GUC CUCUCCAC GGCAAUUU CUUAGCU GUU CAUGUCUU CCUUCAAA GUC CAAGAAGU GGCAACU GCU UUUAUGUU GUC UGGGUGGA GCN GCU UUCUCCA GGCAGCG UGGGACA UGUGACA UVACUCA CUUGUCA UGGAACA UUUCCUCC AGAA GCCCUC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGGUCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUGUUG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AGAA GGAGAA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA GUUGAA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA UNGCAUCA AGAA GAGCCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UAGCAUCA AGAA GAGCCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCAAUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AGAA GAGGCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCUGCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GUGGAGAG AGAA GUCCCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUCACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AAGACAUG AGAA GCUAAG ACCAGAGAAACACGGUUGUGGUACAUUACCUGGUA UUUGAAGG AGAA GAGUAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUUCCA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GACAAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AACAUAAA AGAA GUUGCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA JGGGUCCC AGAA AGAA AGAA AGAA AGAA AGAA AGAA AGAA UGAGUCCC AGUUUCAA CCCCAAGA CACAUAAG UCCACAAA GGUAUAGA AAAUUGCC UCCACCCA ACUUCUUG 5319 5358 5392 5563 5622 5738 5838 5933 6022 6120 6163 6270 6412 6778 6826 7245 6511 ഹ 10 15

512	UUUUCAUG	AGAA	GGAAUU	JUUUCAUG AGAA GGAAUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	AAUUCCU GUC CAUGAAAA
909	GACAUUCA	AGAA	GAAAUG	SACAUUCA AGAA GAAAUG ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CAUJUCA GCC UGAAUGUC
618	AAUAUAUA	AGAA	GACAUU	AAUAUAUA AGAA GACAUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	AAUGUCU GCC UAUAUAUU
633	AUACAAAG	AGAA	GAGAAU	AUACAAAG AGAA GAGAAU ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	AUUCUCU GCU CUINGUAII

Table IV: Human KDR VEGF Receptor-Hammerhead Ribozyme and Substrate Sequence

	nt.	HH Ribozyme Sequence	Substrate
5	Posi tion		
3	21	CACAGGGC CUGAUGA X GAA ACGGCCAG	
	33		CUGGCCGUC GCCCUGUG
		UCCACGCA CUGAUGA X GAA AGCCACAG	CUGUGGCUC UGCGUGGA
	56	AACCCACA CUGAUGA X GAA AGGCGGCC	GGCCGCCUC UGUGGGUU
	64	ACUAGGCA CUGAUGA X GAA ACCCACAG	CUGUGGGUU UGCCUAGU
10	65	CACUAGGC CUGAUGA X GAA AACCCACA	UGUGGGUUU GCCUAGUG
	70	AGAAACAC CUGAUGA X GAA AGGCAAAC	GUUUGCCUA GUGUUUCU
	75	UCAAGAGA CUGAUGA X GAA ACACUAGG	CCUAGUGUU UCUCUUGA
	76	AUCAAGAG CUGAUGA X GAA AACACUAG	CUAGUGUUU CUCUUGAU
	77	GAUCAAGA CUGAUGA X GAA AAACACUA	UAGUGUUUC UCUUGAUC
15	79	CAGAUCAA CUGAUGA X GAA AGAAACAC	GUGUUUCUC UUGAUCUG
	81	GGCAGAUC CUGAUGA X GAA AGAGAAAC	GUUUCUCUU GAUCUGCC
	85	CCUGGGCA CUGAUGA X GAA AUCAAGAG	CUCUUGAUC UGCCCAGG
	96	UGUAUGCU CUGAUGA X GAA AGCCUGGG	CCCAGGCUC AGCAUACA
	102	UCUUUUUG CUGAUGA X GAA AUGCUGAG	CUCAGCAUA CAAAAAGA
20	114	AUUGUAAG CUGAUGA X GAA AUGUCUUU	AAAGACAUA CUUACAAU
	117	UUAAUUGU CUGAUGA X GAA AGUAUGUC	GACAUACUU ACAAUUAA
	118	CUUAAUUG CUGAUGA X GAA AAGUAUGU	ACAUACUUA CAAUUAAG
	123	UUAGCCUU CUGAUGA X GAA AUUGUAAG	CUUACAAUU AAGGCUAA
	124	AUUAGCCU CUGAUGA X GAA AAUUGUAA	UUACAAUUA AGGCUAAU
25	130	AGUUGUAU CUGAUGA X GAA AGCCUUAA	UUAAGGCUA AUACAACU
	133	AAGAGUUG CUGAUGA X GAA AUUAGCCU	AGGCUAAUA CAACUCUU
	139	AAUUUGAA CUGAUGA X GAA AGUUGUAU	AUACAACUC UUCAAAUU
	141	GUAAUUUG CUGAUGA X GAA AGAGUUGU	ACAACUCUU CAAAUUAC
	142	AGUAAUUU CUGAUGA X GAA AAGAGUUG	
30	147	CUGCAAGU CUGAUGA X GAA AUUUGAAG	
	148	CCUGCAAG CUGAUGA X GAA AAUUUGAA	
		UCCCCUGC CUGAUGA X GAA AGUAAUUU	

	170	GCCAGUCC	CUGAUGA	Х	GAA	AGUCCCUC	GAGGGACUU	GGACUGGC
	180	UUGGGCCA	CUGAUGA	Х	GAA	AGCCAGUC	GACUGGCUU	UGGCCCAA
	181	AUUGGGCC	CUGAUGA	X	GAA	AAGCCAGU	ACUGGCUUU	GGCCCAAU
	190	ACUCUGAU	CUGAUGA	X	GAA	AUUGGGCC	GGCCCAAUA	AUCAGAGU
5	193	GCCACUCU	CUGAUGA	X	GAA	AUUAUUGG	CCAAUAAUC	AGAGUGGC
	243	UUACAGAA	CUGAUGA	X	GAA	AGGCCAUC	GAUGGCCUC	UUCUGUAA
	245	UCUUACAG	CUGAUGA	X	GAA	AGAGGCCA	UGGCCUCUU	CUGUAAGA
	246	GUCUUACA	CUGAUGA	X	GAA	AAGAGGCC	GGCCUCUUC	UGUAAGAC
	250	GAGUGUCU	CUGAUGA	Х	GAA	ACAGAAGA	UCUUCUGUA	AGACACUC
10	258	GGAAUUGU	CUGAUGA	Х	GAA	AGUGUCUU	AAGACACUC	ACAAUUCC
	264	ACUUUUGG	CUGAUGA	Х	GAA	AUUGUGAG	CUCACAAUU	CCAAAAGU
	265	CACUUUUG	CUGAUGA	X	GAA	AAUUGUGA	UCACAAUUC	CAAAAGUG
	276	UCAUUUCC	CUGAUGA	X	GAA	AUCACUUU	AAAGUGAUC	GGAAAUGA
	296	AGCACUUG	CUGAUGA	X	GAA	AGGCUCCA	UGGAGCCUA	CAAGUGCU
15	305	CCCGGUAG	CUGAUGA	X	GAA	AGCACUUG	CAAGUGCUU	CUACCGGG
	306	UCCCGGUA	CUGAUGA	X	GAA	AAGCACUU	AAGUGCUUC	UACCGGGA
	308	UUUCCCGG	CUGAUGA	Х	GAA	AGAAGCAC	GUGCUUCUA	CCGGGAAA
	32 3	CCGAGGCC	CUGAUGA	X	GAA	AGUCAGUU	AACUGACUU	GGCCUCGG
	32 9	AAAUGACC	CUGAUGA	X	GAA	AGGCCAAG	CUUGGCCUC	GGUCAUUU
20	33 3	ACAUAAAU	CUGAUGA	X	GAA	ACCGAGGC	GCCUCGGUC	AUUUAUGU
	336	UAGACAUA	CUGAUGA	X	GAA	AUGACCGA	UCGGUCAUU	UAUGUCUA
	337	AUAGACAU	CUGAUGA	X	GAA	AAUGACCG	CGGUCAUUU	AUGUCUAU
	338	CAUAGACA	CUGAUGA	X	GAA	AAAUGACC	GGUCAUUUA	UGUCUAUG
	342	UGAACAUA	CUGAUGA	X	GAA	ACAUAAAU	AUUUAUGUC	UAUGUUCA
25	3 4 4	CUUGAACA	CUGAUGA	X	GAA	AGACAUAA	UUAUGUCUA	UGUUCAAG
•	348	UAAUCUUG	CUGAUGA	Х	GAA	ACAUAGAC	GUCUAUGUU	CAAGAUUA
	34 9	GUAAUCUU	CUGAUGA	X	GAA	AACAUAGA	UCUAUGUUC	AAGAUUAC
	35 5	AGAUCUGU	CUGAUGA	X	GAA	AUCUUGAA	UUCAAGAUU	ACAGAUCU
	356	GAGAUCUG	CUGAUGA	X	GAA	AAUCUUGA	UCAAGAUUA	CAGAUCUC
30	362	UAAAUGGA	CUGAUGA	Х	GAA	AUCUGUAA	UUACAGAUC	UCCAUUUA
	364	AAUAAAUG	CUGAUGA	X	GAA	AGAUCUGU	ACAGAUCUC	CAUUUAUU
	368	AAGCAAUA	CUGAUGA	X	GAA	AUGGAGAU	AUCUCCAUU	UAUUGCUU
	369	GAAGCAAU	CUGAUGA	Х	GAA	AAUGGAGA	UCUCCAUUU	AUUGCUUC

	370	AGAAGCAA CUGAUGA X GAA AAAUGGAG	CUCCAUUUA UUGCUUCU
	372	ACAGAAGC CUGAUGA X GAA AUAAAUGG	
	376	ACUAACAG CUGAUGA X GAA AGCAAUAA	
	3 7 7	CACUAACA CUGAUGA X GAA AAGCAAUA	
5	381	UGGUCACU CUGAUGA X GAA ACAGAAGC	
	382	UUGGUCAC CUGAUGA X GAA AACAGAAG	
	39 9	AUGUACAC CUGAUGA X GAA ACUCCAUG	
	404	CAGUAAUG CUGAUGA X GAA ACACGACU	
	408	UUCUCAGU CUGAUGA X GAA AUGUACAC	Chookeog
10	409	GUUCUCAG CUGAUGA X GAA AAUGUACA	TOOGAGAA
	438	AGACAUGG CUGAUGA X GAA AUCACCAC	
	439		======================================
	445	GGACCCGA CUGAUGA X GAA ACAUGGAA	
	447	AUGGACCC CUGAUGA X GAA AGACAUGG	CCAUGUCUC GGGUCCAU
15	452	UUGAAAUG CUGAUGA X GAA ACCCGAGA	UCUCGGGUC CAUUUCAA
	456	AGAUUUGA CUGAUGA X GAA AUGGACCC	GGGUCCAUU UCAAAUCU
	457	GAGAUUUG CUGAUGA X GAA AAUGGACC	GGUCCAUUU CAAAUCUC
	458	UGAGAUUU CUGAUGA X GAA AAAUGGAC	GUCCAUUUC AAAUCUCA
	463	CACGUUGA CUGAUGA X GAA AUUUGAAA	UUUCAAAUC UCAACGUG
20	465	GACACGUU CUGAUGA X GAA AGAUUUGA	UCAAAUCUC AACGUGUC
	473	CACAAAGU CUGAUGA X GAA ACACGUUG	CAACGUGUC ACUUUGUG
	477	CUUGCACA CUGAUGA X GAA AGUGACAC	GUGUCACUU UGUGCAAG
	478	UCUUGCAC CUGAUGA X GAA AAGUGACA	UGUCACUUU GUGCAAGA
	488	UUUCUGGG CUGAUGA X GAA AUCUUGCA	UGCAAGAUA CCCAGAAA
25	503	CAGGAACA CUGAUGA X GAA AUCUCUUU	AAAGAGAUU UGUUCCUG
	504	UCAGGAAC CUGAUGA X GAA AAUCUCUU	AAGAGAUUU GUUCCUGA
	507	CCAUCAGG CUGAUGA X GAA ACAAAUCU	AGAUUUGUU CCUGAUGG
	508	ACCAUCAG CUGAUGA X GAA AACAAAUC	GAUUUGUUC CUGAUGGU
	517	AAUUCUGU CUGAUGA X GAA ACCAUCAG	CUGAUGGUA ACAGAAUU
30	525	UCCCAGGA CUGAUGA X GAA AUUCUGUU	AACAGAAUU UCCUGGGA
	526	GUCCCAGG CUGAUGA X GAA AAUUCUGU	ACAGAAUUU CCUGGGAC
	527	UGUCCCAG CUGAUGA X GAA AAAUUCUG	CAGAAUUUC CUGGGACA
	548	GAAUAGUA CUGAUGA X GAA AGCCCUUC	GAAGGGCUU UACUAUUC

	549	GGAAUAGU	CUGAUGA	x	GAA	AAGCCCUU	AAGGGCUUU	ACUAUUCC
	550	GGGAAUAG	CUGAUGA	х	GAA	AAAGCCCU	AGGGCUUUA	CUAUUCCC
	553	GCUGGGAA	CUGAUGA	х	GAA	AGUAAA GC	GCUUUACUA	UUCCCAGC
	55 5	UAGCUGGG	CUGAUGA	X	GAA	AUAGUAAA	UUUACUAUU	CCCAGCUA
5	556	GUAGCUGG	CUGAUGA	X	GAA	AAUAGUAA	UUACUAUUC	CCAGCUAC
	5 63	UGAUCAUG	CUGAUGA	Х	GAA	AGCUGGGA	UCCCAGCUA	CAUGAUCA
	57 0	GCAUAGCU	CUGAUGA	X	GAA	AUCAUGUA	UACAUGAUC	AGCUAUGC
	575	UGCCAGCA	CUGAUGA	x	GAA	AGCUGAUC	GAUCAGCUA	UGCUGGCA
	588	UCACAGAA	CUGAUGA	Х	GAA	ACCAUGCC	GGCAUGGUC	UUCUGUGA
10	590	CUUCACAG	CUGAUGA	X	GAA	AGACCAUG	CAUGGUCUU	CUGUGAAG
	591	GCUUCACA	CUGAUGA	X	GAA	AAGACCAU	AUGGUCUUC	UGUGAAGC
	606	UCAUCAUU	CUGAUGA	X	GAA	AUUUUUGC	GCAAAAAUU	AAUGAUGA
	607	UUCAUCAU	CUGAUGA	X	GAA	AAUUUUUG	CAAAAAUUA	AUGAUGAA
	619	AGACUGGU	CUGAUGA	X	GAA	ACUUUCAU	AUGAAAGUU	ACCAGUCU
15	620	UAGACUGG	CUGAUGA	x	GAA	AACUUUCA	UGAAAGUUA	CCAGUCUA
	626	ACAUAAUA	CUGAUGA	X	GAA	ACUGG UA A	UUACCAGUC	UAUUAUGU
	628	GUACAUAA	CUGAUGA	X	GAA	AGACUGGU	ACCAGUCUA	UUAUGUAC
	630	AUGUACAU	CUGAUGA	X	GAA	AUAGACUG	CAGUCUAUU	AUGUACAU
	631	UAUGUACA	CUGAUGA	X	GAA	AAUAGACU	AGUCUAUUA	UGUACAUA
20	635	CAACUAUG	CUGAUGA	X	GAA	ACAUAAUA	UAUUAUGUA	CAUAGUUG
	639	ACGACAAC	CUGAUGA	Х	GAA	AUGUACAU	AUGUACAUA	GUUGUCGU
	642	ACAACGAC	CUGAUGA	x	GAA	ACUAUGUA	UACAUAGUU	GUCGUUGU
	645	CCUACAAC	CUGAUGA	X	GAA	ACAACUAU	AUAGUUGUC	GUUGUAGG
	648	UACCCUAC	CUGAUGA	X	GAA	ACGACAAC	GUUGUCGUU	GUAGGGUA
25	651	CUAUACCC	CUGAUGA	Х	GAA	ACAACGAC	GUCGUUGUA	GGGUAUAG
	65 6	AAAUCCUA	CUGAUGA	Х	GAA	ACCCUACA	UGUAGGGUA	UAGGAUUU
	658	AUAAAUCC	CUGAUGA	X	GAA	AUACCCUA	UAGGGUAUA	GGAUUUAU
	663	ACAUCAUA	CUGAUGA	Х	GAA	AUCCUAUA	UAUAGGAUU	UAUGAUGU
	664	CACAUCAU	CUGAUGA	X	GAA	AAUCCUAU	AUAGGAUUU	AUGAUGUG
30	665	CCACAUCA	CUGAUGA	X	GAA	AAAUCCUA	UAGGAUUUA	UGAUGUGG
	675	GGACUCAG	CUGAUGA	X	GAA	ACCACAUC	GAUGUGGUU	CUGAGUCC
	676	CGGACUCA	CUGAUGA	X	GAA	AACCACAU	AUGUGGUUC	UGAGUCCG
	682	AUGAGACG	CUGAUGA	Х	GAA	ACUCAGAA	UUCUGAGUC	CGUCUCAU

WO 97/15662 PCT/US96/17480

	686	UUCCAUGA	CUGAUGA	X	GAA	ACGGACUC	GAGUCCGUC	UCAUGGAA
	688	AAUUCCAU	CUGAUGA	X	GAA	AGACGGAC	GUCCGUCUC	AUGGAAUU
	696	GAUAGUUC	CUGAUGA	X	GAA	AUUCCAUG	CAUGGAAUU	GAACUAUC
	702	CCAACAGA	CUGAUGA	X	GAA	AGUUCAAU	AUUGAACUA	UCUGUUGG
5	704	CUCCAACA	CUGAUGA	X	GAA	AUAGUUCA	UGAACUAUC	UGUUGGAG
	708	υυυυςυςς	CUGAUGA	X	GAA	ACAGAUAG	CUAUCUGUU	GGAGAAAA
	720	UUUAAGAC	CUGAUGA	Х	GAA	AGCUUUUC	GAAAAGCUU	GUCUUAAA
	723	CAAUUUAA	CUGAUGA	X	GAA	ACAAGCUU	AAGCUUGUC	UUAAAUUG
	725	UACAAUUU	CUGAUGA	Х	GAA	AGACAAGC	GCUUGUCUU	AAAUUGUA
10	726	GUACAAUU	CUGAUGA	Х	GAA	AAGACAAG	CUUGUCUUA	AAUUGUAC
	730	UGCUGUAC	CUGAUGA	X	GAA	AUUUAAGA	UCUUAAAUU	GUACAGCA
	733	UCUUGCUG	CUGAUGA	X	GAA	ACAAUUUA	UAAAUUGUA	CAGCAAGA
	750	CCCACAUU	CUGAUGA	X	GAA	AGUUCAGU	ACUGAACUA	AAUGUGGG
	762	UUGAAGUC	CUGAUGA	x	GAA	AUCCCCAC	GUGGGGAUU	GACUUCAA
15	767	CCCAGUUG	CUGAUGA	Х	GAA	AGUCAAUC	GAUUGACUU	CAACUGGG
	768	UCCCAGUU	CUGAUGA	Х	GAA	AAGUCAAU	AUUGACUUC	AACUGGGA
	779	AAGAAGGG	CUGAUGA	х	GAA	AUUCCCAG	CUGGGAAUA	cccuucuu
	784	CUUCGAAG	CUGAUGA	Х	GAA	AGGGUAUU	AAUACCCUU	CUUCGAAG
	785	GCUUCGAA	CUGAUGA	X	GAA	AAGGGUAU	AUACCCUUC	UUCGAAGC
20	787	AUGCUUCG	CUGAUGA	Х	GAA	AGAAGGGU	ACCCUUCUU	CGAAGCAU
	788	GAUGCUUC	CUGAUGA	X	GAA	AAGAAGGG	CCCUUCUUC	GAAGCAUC
	796	CUUAUGCU	CUGAUGA	х	GAA	AUGCUUCG	CGAAGCAUC	AGCAUAAG
	802	AAGUUUCU	CUGAUGA	x	GAA	AUGCUGAU	AUCAGCAUA	AGAAACUU
	810	CGGUUUAC	CUGAUGA	X	GAA	AGUUUCUU	AAGAAACUU	GUAAACCG
25	813	UCUCGGUU	CUGAUGA	X	GAA	ACAAGUUU	AAACUUGUA	AACCGAGA
	825	UGGGUUUU	CUGAUGA	X	GAA	AGGUCUCG	CGAGACCUA	AAAACCCA
	836	CACUCCCA	CUGAUGA	х	GAA	ACUGGGUU	AACCCAGUC	UGGGAGUG
	857	UGCUCAAA	CUGAUGA	X	GAA	AUUUCUUC	GAAGAAAUU	UUUGAGCA
	858	GUGCUCAA	CUGAUGA	X	GAA	AAUUUCUU	AAGAAAUUU	UUGAGCAC
30	859	GGUGCUCA	CUGAUGA	X	GAA	AAAUUUCU	AGAAAUUUU	UGAGCACC
	860	AGGUGCUC	CUGAUGA	X	GAA	AAAAUUUC	GAAAUUUUU	GAGCACCU
	869	CUAUAGUU	CUGAUGA	X	GAA	AGGUGCUC	GAGCACCUU	AACUAUAG
	870	UCUAUAGU	CUGAUGA	X	GAA	AAGGUGCU	AGCACCUUA	ACUAUAGA

	874	ACCAUCUA	CUGAUGA	X	GAA	AGUUAAGG	CCUUAACUA	UAGAUGGU
	876	ACACCAUC	CUGAUGA	X	GAA	AUAGUUAA	UUAACUAUA	GAUGGUGU
	885	CUCCGGGU	CUGAUGA	X	GAA	ACACCAUC	GAUGGUGUA	ACCCGGAG
	905	AGGUGUAC	CUGAUGA	x	GAA	AUCCUUGG	CCAAGGAUU	GUACACCU
5	908	CACAGGUG	CUGAUGA	x	GAA	ACAAUCCU	AGGAUUGUA	CACCUGUG
	923	GCCCACUG	CUGAUGA	x	GAA	AUGCUGCA	UGCAGCAUC	CAGUGGGC
	956	CCCUGACA	CUGAUGA	x	GAA	AUGUGCUG	CAGCACAUU	UGUCAGGG
	957	ACCCUGAC	CUGAUGA	X	GAA	AAUGUGCU	AGCACAUUU	GUCAGGGU
	960	UGGACCCU	CUGAUGA	х	GAA	ACAAAUGU	ACAUUUGUC	AGGGUCCA
10	966	UUUUCAUG	CUGAUGA	х	GAA	ACCCUGAC	GUCAGGGUC	CAUGAAAA
	9 79	AGCAACAA	CUGAUGA	X	GAA	AGGUUUUU	AAAAACCUU	UUGUUGCU
	980	AAGCAACA	CUGAUGA	X	GAA	AAGGUUUU	AAAACCUUU	UGUUGCUU
	981	AAAGCAAC	CUGAUGA	X	GAA	AAAGGUUU	AAACCUUUU	GUUGCUUU
	984	CCAAAAGC	CUGAUGA	x	GAA	ACAAAAGG	CCUUUUGUU	GCUUUUGG
15	988	ACUUCCAA	CUGAUGA	х	GAA	AGCAACAA	UUGUUGCUU	UUGGAAGU
	989	CACUUCCA	CUGAUGA	х	GAA	AAGCAACA	UGUUGCUUU	UGGAAGUG
	990	CCACUUCC	CUGAUGA	X	GAA	AAAGCAAC	GUUGCUUUU	GGAAGUGG
	1007	CCACCAGA	CUGAUGA	X	GAA	AUUCCAUG	CAUGGAAUC	UCUGGUGG
	1009	UUCCACCA	CUGAUGA	Х	GAA	AGAUUCCA	UGGAAUCUC	UGGUGGAA
20	1038	GGGAUUCU	CUGAUGA	Х	GAA	ACACGCUC	GAGCGUGUC	AGAAUCCC
	1044	UUCGCAGG	CUGAUGA	Х	GAA	AUUCUGAC	GUCAGAAUC	CCUGCGAA
	1055	AACCAAGG	CUGAUGA	Х	GAA	ACUUCGCA	UGCGAAGUA	CCUUGGUU
	1059	GGGUAACC	CUGAUGA	Х	GAA	AGGUACUU	AAGUACCUU	GGUUACCC
	1063	GGGUGGGU	CUGAUGA	Х	GAA	ACCAAGGU	ACCUUGGUU	ACCCACCC
25	1064					AACCAAGG	CCUUGGUUA	CCCACCCC
	1080	UACCAUUU	CUGAUGA	Х	GAA	AUUUCUGG	CCAGAAAUA	AAAUGGUA
	1088	CAUUUUUA	CUGAUGA	Х	GAA	ACCAUUUU	AAAAUGGUA	UAAAAAUG
	1090	UCCAUUUU	CUGAUGA	Х	GAA	AUACCAUU	AAUGGUAUA	AAAAUGGA
	1101	UCAAGGGG	CUGAUGA	Х	GAA	AUUCCAUU	AAUGGAAUA	CCCCUUGA
30	1107	UUGGACUC	CUGAUGA	Х	GAA	AGGGGUAU	AUACCCCUU	GAGUCCAA
	1112					ACUCAAGG	CCUUGAGUC	CAAUCACA
	1117					AUUGGACU	AGUCCAAUC	ACACAAUU
	1125	CCCGCUUU	CUGAUGA	Х	GAA	AUUGUGUG	CACACAAUU	AAAGCGGG

	1126	CCCCGCUU	CUGAUGA	Х	GAA	AAUUGUGU	ACACAAUU	AAGCGGGG
	1140	AUCGUCAG	CUGAUGA	Х	GAA	ACAUGCCC	GGGCAUGUA	CUGACGAU
	1149	ACUUCCAU	CUGAUGA	. X	GAA	AUCGUCAG	CUGACGAUU	AUGGAAGU
	1150	CACUUCCA	CUGAUGA	X	GAA	AAUCGUCA	UGACGAUUA	UGGAAGUG
5	1180	GACAGUGU	CUGAUGA	X	GAA	AUUUCCUG	CAGGAAAUU	ACACUGUC
	1181	UGACAGUG	CUGAUGA	X	GAA	AAUUUCCU	AGGAAAUUA	CACUGUCA
	1188	GUAAGGAU	CUGAUGA	X	GAA	ACAGUGUA	UACACUGUC	AUCCUUAC
	1191	UUGGUAAG	CUGAUGA	X	GAA	AUGACAGU	ACUGUCAUC	CUUACCAA
	1194	GGAUUGGU	CUGAUGA	Х	GAA	AGGAUGAC	GUCAUCCUU	ACCAAUCC
10	1195	GGGAUUGG	CUGAUGA	X	GAA	AAGGAUGA	UCAUCCUUA	CCAAUCCC
	1201	UGAAAUGG	CUGAUGA	Х	GAA	AUUGGUAA	UUACCAAUC	CCAUUUCA
	1206	UCCUUUGA	CUGAUGA	X	GAA	AUGGGAUU	AAUCCCAUU	UCAAAGGA
	1207	CUCCUUUG	CUGAUGA	X	GAA	AAUGGGAU	AUCCCAUUU	CAAAGGAG
	1208	ucuccuuu	CUGAUGA	X	GAA	AAAUGGGA	UCCCAUUUC	AAAGGAGA :
1 5	1233	ACCAGAGA	CUGAUGA	X	GAA	ACCACAUG	CAUGUGGUC	UCUCUGGU
	1235	CAACCAGA	CUGAUGA	X	GAA	AGACCACA	UGUGGUCUC	UCUGGUUG
	1237	CACAACCA	CUGAUGA	X	GAA	AGAGACCA	UGGUCUCUC	UGGUUGUG
	1242	ACAUACAC	CUGAUGA	X	GAA	ACCAGAGA	UCUCUGGUU	GUGUAUGU
	1247	GUGGGACA	CUGAUGA	X	GAA	ACACAACC	GGUUGUGUA	UGUCCCAC
20	1251	UGGGGUGG	CUGAUGA	X	GAA	ACAUACAC	GUGUAUGUC	CCACCCCA
	1263	UUCUCACC	CUGAUGA	Х	GAA	AUCUGGGG	CCCCAGAUU	GGUGAGAA
	1274	AGAUUAGA	CUGAUGA	Х	GAA	AUUUCUCA	UGAGAAAUC	UCUAAUCU
	1276	AGAGAUUA	CUGAUGA	X	GAA	AGAUUUCU	AGAAAUCUC	UAAUCUCU
	1278	GGAGAGAU	CUGAUGA	Х	GAA	AGAGAUUU	AAAUCUCUA	AUCUCUCC
25	1281	ACAGGAGA	CUGAUGA	x	GAA	AUUAGAGA	UCUCUAAUC	UCUCCUGU
	1283	CCACAGGA	CUGAUGA	X	GAA	AGAUUAGA	UCUAAUCUC	UCCUGUGG
	1285	AUCCACAG	CUGAUGA	X	GAA	AGAGAUUA	UAAUCUCUC	CUGUGGAU
	1294	CUGGUAGG	CUGAUGA	X	GAA	AUCCACAG	CUGUGGAUU	CCUACCAG
	1295	ACUGGUAG	CUGAUGA	X	GAA	AAUCCACA	UGUGGAUUC	CUACCAGU
30	1298	CGUACUGG	CUGAUGA	X	GAA	AGGAAUCC	GGAUUCCUA	CCAGUACG
	1304	UGGUGCCG	CUGAUGA	X	GAA	ACUGGUAG	CUACCAGUA	CGGCACCA
	1315	CAGCGUUU	CUGAUGA	X	GAA	AGUGGUGC	GCACCACUC	AAACGCUG
	1330	AUAGACCG	CUGAUGA	Х	GAA	ACAUGUCA	UGACAUGUA	CGGUCUAU

	1335	AUGGCAUA	CUGAUGA	х	GAA	ACCGUACA	UGUACGGUC	UAUGCCAU
	1337	GAAUGGCA	CUGAUGA	X	GAA	AGACCGUA	UACGGUCUA	UGCCAUUC
	1344	GGGGGAGG	CUGAUGA	X	GAA	AUGGCAUA	UAUGCCAUU	CCUCCCCC
	1345	CGGGGGAG	CUGAUGA	х	GAA	AAUGGCAU	AUGCCAUUC	CUCCCCCG
5	1348	AUGCGGGG	CUGAUGA	x	GAA	AGGAAUGG	CCAUUCCUC	CCCCGCAU
	1357	GUGGAUGU	CUGAUGA	x	GAA	AUGCGGGG	CCCCGCAUC	ACAUCCAC
	1362	UACCAGUG	CUGAUGA	X	GAA	AUGUGAUG	CAUCACAUC	CACUGGUA
	1370	ACUGCCAA	CUGAUGA	X	GAA	ACCAGUGG	CCACUGGUA	UUGGCAGU
	1372	CAACUGCC	CUGAUGA	X	GAA	AUACCAGU	ACUGGUAUU	GGCAGUUG
10	1379	CUUCCUCC	CUGAUGA	х	GAA	ACUGCCAA	UUGGCAGUU	GGAGGAAG
	1416	GUCACUGA	CUGAUGA	x	GAA	ACAGCUUG	CAAGCUGUC	UCAGUGAC
	1418	UUGUCACU	CUGAUGA	x	GAA	AGACAGCU	AGGUGUCUC	AGUGACAA
	1433	CACAAGGG	CUGAUGA	x	GAA	AUGGGUUU	AAACCCAUA	CCCUUGUG
	1438	UUCUUCAC	CUGAUGA	x	GAA	AGGGUAUG	CAUACCCUU	GUGAAGAA
15	1466	CUCCCUGG	CUGAUGA	Х	GAA	AGUCCUCC	GGAGGACUU	CCAGGGAG
	1467	CCUCCCUG	CUGAUGA	X	GAA	AAGUCCUC	GAGGACUUC	CAGGGAGG
	1480	UUCAAUUU	CUGAUGA	X	GAA	AUUUCCUC	GAGGAAAUA	AAAUUGAA
	1485	UUAACUUC	CUGAUGA	х	GAA	UUAUUU	UUAAAAUA	GAAGUUAA
	1491	UUUUUUUU	CUGAUGA	X	GAA	ACUUCAAU	AUUGAAGUU	AAUAAAA
20	1492	UAUUUUUA	CUGAUGA	Х	GAA	AACUUCAA	UUGAAGUUA	AUAAAAAU
	1495	UUGAUUUU	CUGAUGA	Х	GAA	AUUAACUU	AAGUUAAUA	AAAAUCAA
	1501	AGCAAAUU	CUGAUGA	Х	GAA	UAUUUUUA	AUAAAAAUC	AAUUUGCU
	1505	UUAGAGCA	CUGAUGA	X	GAA	AUUGAUUU	AAAUCAAUU	UGCUCUAA
	1506	AUUAGAGC	CUGAUGA	x	GAA	AAUUGAUU	AAUCAAUUU	GCUCUAAU
25	1510	UUCAAUUA	CUGAUGA	х	GAA	AGCAAAUU	AAUUUGCUC	UAAUUGAA
	1512	CCUUCAAU	CUGAUGA	X	GAA	AGAGCAAA	UUUGCUCUA	AUUGAAGG
	1515	UUUCCUUC	CUGAUGA	Х	GAA	AUUAGAGC	GCUCUAAUU	GAAGGAAA
	1536	AGGGUACU	CUGAUGA	Х	GAA	ACAGUUUU	AAAACUGUA	AGUACCCU
	1540	AACAAGGG	CUGAUGA	X	GAA	ACUUACAG	CUGUAAGUA	cccuuguu
30	1545	UGGAUAAC	CUGAUGA	х	GAA	AGGGUACU	AGUACCCUU	GUUAUCCA
	1548	GCUUGGAU	CUGAUGA	X	GAA	ACAAGGGU	ACCCUUGUU	AUCCAAGC
•	1549	CGCUUGGA	CUGAUGA	X	GAA	AACAAGGG	CCCUUGUUA	UCCAAGCG
	1551	GCCGCUUG	CUGAUGA	X	GAA	AUAACAAG	CUUGUUAUC	CAAGCGGC

	1568	ACAAAGCU	CUGAUGA	λ Σ	GA/	A ACACAUUU	AAAUGUGUC AGCUUUGU
	1573	UUUGUACA	CUGAUGA	X	GA/	A AGCUGACA	UGUCAGCUU UGUACAAA
	1574	AUUUGUAC	CUGAUGA	X	GA/	AAGCUGAC	GUCAGCUUU GUACAAAU
	1577	CACAUUUG	CUGAUGA	Х	GAA	ACAAAGCU	AGCUUUGUA CAAAUGUG
5	1593	ACUUUGUU	CUGAUGA	X	GAA	ACCGCUUC	GAAGCGGUC AACAAAGU
	1602	CCUCUCCC	CUGAUGA	X	GAA	ACUUUGUU	AACAAAGUC GGGAGAGG
	1623	UGGAAGGA	CUGAUGA	X	GAA	AUCACCCU	AGGGUGAUC UCCUUCCA
	1625	CGUGGAAG	CUGAUGA	X	GAA	AGAUCACC	GGUGAUCUC CUUCCACG
	1628	UCACGUGG	CUGAUGA	. x	GAA	AGGAGAUC	GAUCUCCUU CCACGUGA
10	1629	GUCACGUG	CUGAUGA	X	GAA	AAGGAGAU	AUCUCCUUC CACGUGAC
	1645	AAUUUCAG	CUGAUGA	X	GAA	ACCCCUGG	CCAGGGGUC CUGAAAUU
	1653	UGCAAAGU	CUGAUGA	X	GAA	AUUUCAGG	CCUGAAAUU ACUUUGCA
	1654	UUGCAAAG	CUGAUGA	X	GAA	AAUUUCAG	CUGAAAUUA CUUUGCAA
	1657	AGGUUGCA	CUGAUGA	х	GAA	AGUAAUUU	AAAUUACUU UGCAACCU
15	1658	CAGGUUGC	CUGAUGA	X	GAA	AAGUAAUU	AAUUACUUU GCAACCUG
	1697	ACCACAAA	CUGAUGA	X	GAA	ACACGCUC	GAGCGUGUC UUUGUGGU
	1699	GCACCACA	CUGAUGA	X	GAA	AGACACGC	GCGUGUCUU UGUGGUGC
	1700	UGCACCAC	CUGAUGA	x	GAA	AAGACACG	CGUGUCUUU GUGGUGCA
	1721	CAAACGUA	CUGAUGA	x	GAA	AUCUGUCU	AGACAGAUC UACGUUUG
20	1723	CUCAAACG	CUGAUGA	х	GAA	AGAUCUGU	ACAGAUCUA CGUUUGAG
	1727	GGUUCUCA	CUGAUGA	Х	GAA	ACGUAGAU	AUCUACGUU UGAGAACC
	1728	AGGUUCUC	CUGAUGA	X	GAA	AACGUAGA	UCUACGUUU GAGAACCU
	1737	UACCAUGU (CUGAUGA	X	GAA	AGGUUCUC	GAGAACCUC ACAUGGUA
	1745	CAAGCUUG	CUGAUGA	X	GAA	ACCAUGUG	CACAUGGUA CAAGCUUG
25	1752	UGUGGGCC (CUGAUGA	X	GAA	AGCUUGUA	UACAAGCUU GGCCCACA
	1765	GAUUGGCA (CUGAUGA	X	GAA	AGGCUGUG	CACAGCCUC UGCCAAUC
	1773	CCCACAUG (CUGAUGA	X	GAA	AUUGGCAG	CUGCCAAUC CAUGUGGG
	1787	GUGUGGGC (CUGAUGA	X	GAA	ACUCUCCC	GGGAGAGUU GCCCACAC
	1800	UUCUUGCA (CUGAUGA	X	GAA	ACAGGUGU	ACACCUGUU UGCAAGAA
30	1801	GUUCUUGC (CUGAUGA	X	GAA	AACAGGUG	CACCUGUUU GCAAGAAC
	1811	GAGUAUCC C	UGAUGA	X	GAA	AGUUCUUG	CAAGAACUU GGAUACUC
	1816	CCAAAGAG C	UGAUGA	X	GAA	AUCCAAGU	ACUUGGAUA CUCUUUGG
	1819	UUUCCAAA C	UGAUGA	X	GAA	AGUAUCCA	UGGAUACUC UUUGGAAA

	1821	AAUUUCCA	CUGAUGA	X	GAA	AGAGUAUC	GAUACUCUU	UGGAAAUU
	1822	CAAUUUCC	CUGAUGA	Х	GAA	AAGAGUAU	AUACUCUUU	GGAAAUUG
	1829	UGGCAUUC	CUGAUGA	X	GAA	AUUUCCAA	UUGGAAAUU	GAAUGCCA
	1844	UAUUAGAG	CUGAUGA	X	GAA	ACAUGGUG	CACCAUGUU	CUCUAAUA
5	1845	CUAUUAGA	CUGAUGA	X	GAA	AACAUGGU	ACCAUGUUC	UCUAAUAG
	1847	UGCUAUUA	CUGAUGA	X	GAA	AGAACAUG	CAUGUUCUC	UAAUAGCA
	1849	UGUGCUAU	CUGAUGA	X	GAA	AGAGAACA	UGUUCUCUA	AUAGCACA
	1852	AUUUGUGC	CUGAUGA	X	GAA	AUUAGAGA	UCUCUAAUA	GCACAAAU
	1866	AUGAUCAA	CUGAUGA	x	GAA	AUGUCAUU	AAUGACAUU	UUGAUCAU
10	1867	CAUGAUCA	CUGAUGA	X	GAA	AAUGUCAU	AUGACAUUU	UGAUCAUG
	1868	CCAUGAUC	CUGAUGA	X	GAA	AAAUGUCA	UGACAUUUU	GAUCAUGG
	1872	AGCUCCAU	CUGAUGA	х	GAA	AUCAAAAU	AUUUUGAUC	AUGGAGCU
	1881	GCAUUCUU	CUGAUGA	Х	GAA	AGCUCCAU	AUGGAGCUU	AAGAAUGC
	1882	UGCAUUCU	CUGAUGA	X	GAA	AAGCUCCA	UGGAGCUUA	AGAAUGCA
1 5	1892	CCUGCAAG	CUGAUGA	x	GAA	AUGCAUUC	GAAUGCAUC	CUUGCAGG
	1895	GGUCCUGC	CUGAUGA	X	GAA	AGGAUGCA	UGCAUCCUU	GCAGGACC
	1913	GGCAGACA	CUGAUGA	X	GAA	AGUCUCCU	AGGAGACUA	UGUCUGCC
	1917	GCAAGGCA	CUGAUGA	X	GAA	ACAUAGUC	GACUAUGUC	UGCCUUGC
	1923	UCUUGAGC	CUGAUGA	X	GAA	AGGCAGAC	GUCUGCCUU	GCUCAAGA
20	1927	CCUGUCUU	CUGAUGA	X	GAA	AGCAAGGC	GCCUUGCUC	AAGACAGG
	1954	GACCACGC	CUGAUGA	X	GAA	AUGUCUUU	AAAGACAUU	GCGUGGUC
	1962	AGCUGCCU	CUGAUGA	X	GAA	ACCACGCA	UGCGUGGUC	AGGCAGCU
	1971	AGGACUGU	CUGAUGA	X	GAA	AGCUGCCU	AGGCAGCUC	ACAGUCCU
	1977	CGCUCUAG	CUGAUGA	X	GAA	ACUGUGAG	CUCACAGUC	CUAGAGCG
25	1980	ACACGCUC	CUGAUGA	X	GAA	AGGACUGU	ACAGUCCUA	GAGCGUGU
	2001	UUUCCUGU	CUGAUGA	X	GAA	AUCGU GG G	CCCACGAUC	ACAGGAAA
	2020	UGUCGUCU	CUGAUGA	X	GAA	AUUCUCCA	UGGAGAAUC	AGACGACA
	2032	UUCCCCAA	CUGAUGA	Х	GAA	ACUUGUCG	CGACAAGUA	UUGGGGAA
	2034	CUUUCCCC	CUGAUGA	X	GAA	AUACUUGU	ACAAGUAUU	GGGGAAAG
30	2046	GAGACUUC	CUGAUGA	Х	GAA	AUGCUUUC	GAAAGCAUC	GAAGUCUC
	2052	GUGCAUGA	CUGAUGA	X	GAA	ACUUCGAU	AUCGAAGUC	UCAUGCAC
	2054	CCGUGCAU	CUGAUGA	X	GAA	AGACUUCG	CGAAGUCUC	AUGCACGG
	2066	GAUUCCCA	CUGAUGA	Χ	GAA	AUGCCGUG	CACGGCAUC	UGGGAAUC

	2074	UGGAGGG	CUGAUGA	Α >	GA/	A AUUCCCAG	CUGGGAAUC	CCCCUCCA
	2080	GAUCUGUG	G CUGAUGA	X A	GA,	A AGGGGGAU	AUCCCCCUC	CACAGAUC
	2088	AACCACAU	J CUGAUGA	A X	GA,	A AUCUGUGG	CCACAGAUC	AUGUGGUU
	2096	UAUCUUUA	CUGAUGA	Х	GA	ACCACAUG	CAUGUGGUU	UAAAGAUA
5	2097	UUAUCUUU	J CUGAUGA	Х	GAA	AACCACAU	AUGUGGUUU	AAAGAUAA
	2098	AUUAUCUU	CUGAUGA	X	GAA	AAACCACA	UGUGGUUUA	AAGAUAAU
	2104	GGUCUCAU	CUGAUGA	X	GAA	AUCUUUAA	UUAAAGAUA	AUGAGACC
	2115	UCUUCUAC	CUGAUGA	X	GAA	AGGGUCUC	GAGACCCUU	GUAGAAGA
	2118	GAGUCUUC	CUGAUGA	X	GAA	ACAAGGGU	ACCCUUGUA	GAAGACUC
10	2126	CAAUGCCU	CUGAUGA	X	GAA	AGUCUUCU	AGAAGACUC	AGGCAUUG
	2133	UUCAAUAC	CUGAUGA	X	GAA	AUGCCUGA	UCAGGCAUU	GUAUUGAA
	2136	UCCUUCAA	CUGAUGA	X	GAA	ACAAUGCC	GGCAUUGUA	UUGAAGGA
	2138	CAUCCUUC	CUGAUGA	x	GAA	AUACAAUG	CAUUGUAUU	GAAGGAUG
	2160	CGGAUAGU	CUGAUGA	x	GAA	AGGUUCCG	CGGAACCUC	ACUAUCCG
15	2164	UCUGCGGA	CUGAUGA	x	GAA	AGUGAGGU	ACCUCACUA	UCCGCAGA
	2166	ACUCUGCG	CUGAUGA	X	GAA	AUAGUGAG	CUCACUAUC	CGCAGAGU
	2196	CAGGUGUA	CUGAUGA	X	GAA	AGGCCUUC	GAAGGCCUC	UACACCUG
	2198	GGCAGGUG	CUGAUGA	X	GAA	AGAGGCCU	AGGCCUCUA	CACCUGCC
	2220	CAGCCAAG	CUGAUGA	х	GAA	ACACUGCA	UGCAGUGUU	CUUGGCUG
20	2221	ACAGCCAA	CUGAUGA	х	GAA	AACACUGC	GCAGUGUUC	UUGGCUGU
	2223	GCACAGCC	CUGAUGA	Х	GAA	AGAACACU	AGUGUUCUU	GGCUGUGC
	2246	UUAUGAAA	CUGAUGA	Х	GAA	AUGCCUCC	GGAGGCAUU	UUUCAUAA
	2247	AUUAUGAA	CUGAUGA	X	GAA	AAUGCCUC	GAGGCAUUU	UUCAUAAU
	2248	UAUUAUGA	CUGAUGA	X	GAA	AAAUGCCU	AGGCAUUUU	UCAUAAUA
25	2249	CUAUUAUG	CUGAUGA	х	GAA	AAAAUGCC	GGCAUUUUU	CAUAAUAG
	2250	UCUAUUAU	CUGAUGA	х	GAA	AAAAAUGC	GCAUUUUUC	AUAAUAGA
	2253	CCUUCUAU	CUGAUGA	x	GAA	AUGAAAAA	UUUUUCAUA .	AUAGAAGG
	2256	GCACCUUC	CUGAUGA	x	GAA	AUUAUGAA	UUCAUAAUA	GAAGGUGC
	2282	UGAUUUCC	CUGAUGA	x	GAA	AGUUCGUC	GACGAACUU (GGAAAUCA
30	2289	AGAAUAAU	CUGAUGA	X	GAA	AUUUCCAA	UUGGAAAUC .	AUUAUUCU
	2292	ACUAGAAU	CUGAUGA	X	GAA	AUGAUUUC	GAAAUCAUU 2	AUUCUAGU
	2293	UACUAGAA	CUGAUGA	X	GAA	AAUGAUUU	AAAUCAUUA (JUCUAGUA
	229 5	CCUACUAG	CUGAUGA	Х	GAA	AUAAUGAU	AUCAUUAUU (CUAGUAGG

	2296	GCCUACUA	CUGAUGA	X	GAA	AAUAAUGA	UCAUUAUUC	UAGUAGGC
	2298	GUGCCUAC	CUGAUGA	x	GAA	AGAAUAAU	AUUAUUCUA	GUAGGCAC
	2301	GUCGUGCC	CUGAUGA	X	GAA	ACUAGAAU	AUUCUAGUA	GGCACGAC
	2316	AACAUGGC	CUGAUGA	X	GAA	AUCACCGU	ACGGUGAUU	GCCAUGUU
5	2324	GCCAGAAG	CUGAUGA	X	GAA	ACAUGGCA	UGCCAUGUU	CUUCUGGC
	2325	AGCCAGAA	CUGAUGA	x	GAA	AACAUGGC	GCCAUGUUC	UUCUGGCU
	2327	GUAGCCAG	CUGAUGA	х	GAA	AGAACAUG	CAUGUUCUU	CUGGCUAC
	2328	AGUAGCCA	CUGAUGA	х	GAA	AAGAACAU	AUGUUCUUC	UGGCUACU
	2334	ACAAGAAG	CUGAUGA	X	GAA	AGCCAGAA	UUCUGGCUA	CUUCUUGU
10	2337	AUGACAAG	CUGAUGA	X	GAA	AGUAGCCA	UGGCUÁCUU	CUUGUCAU
	2338	GAUGACAA	CUGAUGA	Х	GAA	AAGUAGCC	GGCUACUUC	UUGUCAUC
	2340	AUGAUGAC	CUGAUGA	x	GAA	AGAAGUAG	CUACUUCUU	GUCAUCAU
	2343	AGGAUGAU	CUGAUGA	x	GAA	ACAAGAAG	CUUCUUGUC	AUCAUCCU
	2346	CCUAGGAU	CUGAUGA	X	GAA	AUGACAAG	CUUGUCAUC	AUCCUAGG
15	2349	GUCCCUAG	CUGAUGA	Х	GAA	AUGAUGAC	GUCAUCAUC	CUAGGGAC
	2352	ACGGUCCC	CUGAUGA	х	GAA	AGGAUGAU	AUCAUCCUA	GGGACCGU
	2361	GCCCGCUU	CUGAUGA	Х	GAA	ACGGUCCC	GGGACCGUU	AAGCGGGC
	2362	GGCCCGCU	CUGAUGA	X	GAA	AACGGUCC	GGACCGUUA	AGCGGGCC
	2396	UGGACAAG	CUGAUGA	Х	GAA	AGCCUGUC	GACAGGCUA	CUUGUCCA
20	239 9	CGAUGGAC	CUGAUGA	X	GAA	AGUAGCCU	AGGCUACUU	GUCCAUCG
	2402	UGACGAUG	CUGAUGA	х	GAA	ACAAGUAG	CUACUUGUC	CAUCGUCA
	2406	UCCAUGAC	CUGAUGA	X	GAA	AUGGACAA	UUGUCCAUC	GUCAUGGA
	2409	GGAUCCAU	CUGAUGA	X	GAA	ACGAUGGA	UCCAUCGUC	AUGGAUCC
	2416	UUCAUCUG	CUGAUGA	X	GAA	AUCCAUGA	UCAUGGAUC	CAGAUGAA
25	2427	UCCAAUGG	CUGAUGA	X	GAA	AGUUCAUC	GAUGAACUC	CCAUUGGA
	2432	GUUCAUCC	CUGAUGA	X	GAA	AUGGGAGU	ACUCCCAUU	GGAUGAAC
	2443	UCGUUCAC	CUGAUGA	Х	GAA	AUGUUCAU	AUGAACAUU	GUGAACGA
	2458	GGCAUCAU	CUGAUGA	X	GAA	AGGCAGUC	GACUGCCUU	AUGAUGCC
	2459	UGGCAUCA	CUGAUGA	X	GAA	AAGGCAGU	ACUGCCUUA	UGAUGCCA
30	2480	CUCUGGGG	CUGAUGA	X	GAA	AUUCCCAU	AUGGGAAUU	CCCCAGAG
	2481	UCUCUGGG	CUGAUGA	X	GAA	AAUUCCCA	UGGGAAUUC	CCCAGAGA
	2502	GGCUUACC	CUGAUGA	X	GAA	AGGUUCAG	CUGAACCUA	GGUAAGCC
	2506	AAGAGGCU	CUGAUGA	X	GAA	ACCUAGGU	ACCUAGGUA	AGCCUCUU

	2512	ACGGCCAA	CUGAUGA	X	GAA	AGGCUUAC	GUAAGCCUC	UUGGCCGU
	2514	CCACGGCC	CUGAUGA	Х	GAA	AGAGGCUU	AAGCCUCUU	GGCCGUGG
	2528	CUUGGCCA	CUGAUGA	X	GAA	AGGCACCA	UGGUGCCUU	UGGCCAAG
	2529	UCUUGGCC	CUGAUGA	X	GAA	AAGGCACC	GGUGCCUUU	GGCCAAGA
5	2541	UCUGCUUC	CUGAUGA	X	GAA	AUCUCUUG	CAAGAGAUU	GAAGCAGA
	2555	CAAUUCCA	CUGAUGA	X	GAA	AGGCAUCU	AGAUGCCUU	UGGAAUUG
	2556	UCAAUUCC	CUGAUGA	Х	GAA	AAGGCAUC	GAUGCCUUU	GGAAUUGA
	2562	GUCUUGUC	CUGAUGA	X	GAA	AUUCCAAA	UUUGGAAUU	GACAAGAC
	2578	UGUCCUGC	CUGAUGA	x	GAA	AGUUGCUG	CAGCAACUU	GCAGGACA
10	2589	UUGACUGC	CUGAUGA	x	GAA	ACUGUCCU	AGGACAGUA	GCAGUCAA
	2595	AACAUUUU	CUGAUGA	x	GAA	ACUGCUAC	GUAGCAGUC	AAAAUGUU
•	2603	CUUCUUUC	CUGAUGA	X	GAA	ACAUUUUG	CAAAAUGUU	GAAAGAAG
	2632	GAGAGCUC	CUGAUGA	X	GAA	AUGCUCAC	GUGAGCAUC	GAGCUCUC
	2638	AGACAUGA	CUGAUGA	x	GAA	AGCUCGAU	AUCGAGCUC	UCAUGUCU
15	2640	UCAGACAU	CUGAUGA	x	GAA	AGAGCUCG	CGAGCUCUC	AUGUCUGA
	2645	UGAGUUCA	CUGAUGA	X	GAA	ACAUGAGA	UCUCAUGUC	UGAACUCA
	2652	AGGAUCUU	CUGAUGA	x	GAA	AGUUCAGA	UCUGAACUC	AAGAUCCU
	2658	UGAAUGAG	CUGAUGA	x	GAA	AUCUUGAG	CUCAAGAUC	CUCAUUCA
	2661	AUAUGAAU	CUGAUGA	x	GAA	AGGAUCUU	AAGAUCCUC	AUUCAUAU
20	2664	CCAAUAUG	CUGAUGA	х	GAA	AUGAGGAU	AUCCUCAUU	CAUAUUGG
	2665	ACCAAUAU	CUGAUGA	x	GAA	AAUGAGGA	UCCUCAUUC	AUAUUGGU
	2668	GUGACCAA	CUGAUGA	x	GAA	AUGAAUGA	UCAUUCAUA	UUGGUCAC
	2670	UGGUGACC	CUGAUGA	X	GAA	AUAUGAAU	AUUCAUAUU	GGUCACCA
	2674	GAGAUGGU	CUGAUGA	X	GAA	ACCAAUAU	AUAUUGGUC	ACCAUCUC
25	2680	CACAUUGA	CUGAUGA	x	GAA	AUGGUGAC	GUCACCAUC	UCAAUGUG
	2682	ACCACAUU	CUGAUGA	x	GAA	AGAUGGUG	CACCAUCUC	AAUGUGGU
	2691	AGAAGGUU	CUGAUGA	x	GAA	ACCACAUU	AAUGUGGUC	AACCUUCU
	2697	GCACCUAG	CUGAUGA	X	GAA	AGGUUGAC	GUCAACCUU	CUAGGUGC
٠	2698	GGCACCUA	CUGAUGA	X	GAA	AAGGUUGA	UCAACCUUC	UAGGUGCC
30	2700	CAGGCACC	CUGAUGA	X	GAA	AGAAGGUU	AACCUUCUA	GGUGCCUG
	2710	UGGCUUGG	CUGAUGA	X	GAA	ACAGGCAC	GUGCCUGUA	CCAAGCCA
	2730	AUCACCAU	CUGAUGA	X	GAA	AGUGGCCC	GGGCCACUC	AUGGUGAU
	2739	AAUUCCAC	CUGAUGA	X	GAA	AUCACCAU	AUGGUGAUU	GUGGAAUU

	2747	AUUUGCAG	CUGAUGA	X	GAA	AUUCCACA	UGUGGAAUU	CUGCAAAU
	2748	AAUUUGCA	CUGAUGA	X	GAA	AAUUCCAC	GUGGAAUUC	UGCAAAUU
	2756	GGUUUCCA	CUGAUGA	X	GAA	AUUUGCAG	CUGCAAAUU	UGGAAACC
	2757	AGGUUUCC	CUGAUGA	X	GAA	AAUUUGCA	UGCAAAUUU	GGAAACCU
5	2768	GGUAAGUG	CUGAUGA	X	GAA	ACAGGUUU	AAACCUGUC	CACUUACC
	2773	CCUCAGGU	CUGAUGA	X	GAA	AGUGGACA	UGUCCACUU	ACCUGAGG
	2774	UCCUCAGG	CUGAUGA	X	GAA	AAGUGGAC	GUCCACUUA	CCUGAGGA
	2798	AGGGGACA	CUGAUGA	x	GAA	AUUCAUUU	AAAUGAAUU	UGUCCCCU
	2799	UAGGGGAC	CUGAUGA	X	GAA	AAUUCAUU	AAUGAAUUU	GUCCCCUA
10	2802	UUGUAGGG	CUGAUGA	X	GAA	ACAAAUUC	GAAUUUGUC	CCCUACAA
	2807	UGGUCUUG	CUGAUGA	x	GAA	AGGGGACA	UGUCCCCUA	CAAGACCA
	2828	CUUGACGG	CUGAUGA	х	GAA	AUCGUGCC	GGCACGAUU	CCGUCAAG
	2829	CCUUGACG	CUGAUGA	X	GAA	AAUCGUGC	GCACGAUUC	CGUCAAGG
	2833	UUUCCCUU	CUGAUGA	x	GAA	ACGGAAUC	GAUUCCGUC	AAGGGAAA
15	2846	CUCCAACG	CUGAUGA	х	GAA	AGUCUUUC	GAAAGACUA	CGUUGGAG
	2850	AUUGCUCC	CUGAUGA	X	GAA	ACGUAGUC	GACUACGUU	GGAGCAAU
	2859	UCCACAGG	CUGAUGA	X	GAA	AUUGCUCC	GGAGCAAUC	CCUGUGGA
	2869	CCGUUUCA	CUGAUGA	X	GAA	AUCCACAG	CUGUGGAUC	UGAAACGG
	2882	UGCUGUCC	CUGAUGA	X	GAA	AGCGCCGU	ACGGCGCUU	GGACAGCA
20	2892	CUACUGGU	CUGAUGA	Х	GAA	AUGCUGUC	GACAGCAUC	ACCAGUAG
	2899	GCUCUGGC	CUGAUGA	X	GAA	ACUGGUGA	UCACCAGUA	GCCAGAGC
	2909	AGCUGGCU	CUGAUGA	х	GAA	AGCUCUGG	CCAGAGCUC	AGCCAGCU
	2918	CAAAUCCA	CUGAUGA	Х	GAA	AGCUGGCU	AGCCAGCUC	UGGAUUUG
	2924	CCUCCACA	CUGAUGA	X	GAA	AUCCAGAG	CUCUGGAUU	UGUGGAGG
25	2925	UCCUCCAC	CUGAUGA	X	GAA	AAUCCAGA	UCUGGAUUU	GUGGAGGA
	2939	CACUGAGG	CUGAUGA	X	GAA	ACUUCUCC	GGAGAAGUC	CCUCAGUG
	2943	ACAUCACU	CUGAUGA	X	GAA	AGGGACUU	AAGUCCCUC	AGUGAUGU
	2952	UCUUCUUC	CUGAUGA	X	GAA	ACAUCACU	AGUGAUGUA	GAAGAAGA
	2968	AUCUUCAG	CUGAUGA	Х	GAA	AGCUUCCU	AGGAAGCUC	CUGAAGAU
30	2977	CUUAUACA	CUGAUGA	Х	GAA	AUCUUCAG	CUGAAGAUC	UGUAUAAG
	2981	AGUCCUUA	CUGAUGA	Х	GAA	ACAGAUCU	AGAUCUGUA	UAAGGACU
	2983	GAAGUCCU	CUGAUGA	х	GAA	AUACAGAU	AUCUGUAUA	AGGACUUC
	2990	AGGUCAGG	CUGAUGA	X	GAA	AGUCCUUA	UAAGGACUU	CCUGACCU

	2991	AAGGUCAG	CUGAUGA	Х	GAA	AAGUCCUU	AAGGACUUC	CUGACCUU
	2999	GAUGCUCC	CUGAUGA	Х	GAA	AGGUCAGG	CCUGACCUU	GGAGCAUC
	3007	ACAGAUGA	CUGAUGA	X	GAA	AUGCUCCA	UGGAGCAUC	UCAUCUGU
	3009	UAACAGAU	CUGAUGA	X	GAA	AGAUGCUC	GAGCAUCUC	AUCUGUUA
5	3012	CUGUAACA	CUGAUGA	X	GAA	AUGAGAUG	CAUCUCAUC	UGUUACAG
	3016	GAAGCUGU	CUGAUGA	X	GAA	ACAGAUGA	UCAUCUGUU	ACAGCUUC
	3017	GGAAGCUG	CUGAUGA	X	GAA	AACAGAUG	CAUCUGUUA	CAGCUUCC
	3023	CCACUUGG	CUGAUGA	X	GAA	AGCUGUAA	UUACAGCUU	CCAAGUGG
	3024	GCCACUUG	CUGAUGA	X	GAA	AAGCUGUA	UACAGCUUC	CAAGUGGC
10	3034	CAUGCCCU	CUGAUGA	X	GAA	AGCCACUU	AAGUGGCUA	AGGGCAUG
	3047	AUGCCAAG	CUGAUGA	X	GAA	ACUCCAUG	CAUGGAGUU	CUUGGCAU
	3048	GAUGCCAA	CUGAUGA	X	GAA	AACUCCAU	AUGGAGUUC	UUGGCAUC
	3050	GCGAUGCC	CUGAUGA	X	GAA	AGAACUCC	GGAGUUCUU	GGCAUCGC
	3056	ACUUUCGC	CUGAUGA	X	GAA	AUGCCAAG	CUUGGCAUC	GCGAAAGU
15	3067	CCUGUGGA	CUGAUGA	X	GAA	ACACUUUC	GAAAGUGUA	UCCACAGG
	3069	UCCCUGUG	CUGAUGA	X	GAA	AUACACUU	AAGUGUAUC	CACAGGGA
	3094	UAAGAGGA	CUGAUGA	X	GAA	AUUUCGUG	CACGAAAUA	UCCUCUUA
	3096	GAUAAGAG	CUGAUGA	X	GAA	AUAUUUCG	CGAAAUAUC	CUCUUAUC
	3099	UCCGAUAA	CUGAUGA	x	GAA	AGGAUAUU	AAUAUCCUC	UUAUCGGA
20	3101	UCUCCGAU	CUGAUGA	X	GAA	AGAGGAUA	UAUCCUCUU	AUCGGAGA
	3102	UUCUCCGA	CUGAUGA	X	GAA	AAGAGGAU	AUCCUCUUA	UCGGAGAA
	3104	UCUUCUCC	CUGAUGA	X	GAA	AUAAGAGG	CCUCUUAUC	GGAGAAGA
	3120	CAGAUUUU	CUGAUGA	X	GAA	ACCACGUU	AACGUGGUU	AAAAUCUG
	3121	ACAGAUUU	CUGAUGA	X	GAA	AACCACGU	ACGUGGUUA	AAAUCUGU
25	3126	AAGUCACA	CUGAUGA	X	GAA	AUUUUAAC	GUUAAAAUC	UGUGACUU
	3134	CCAAGCCA	CUGAUGA	X	GAA	AGUCACAG	CUGUGACUU	UGGCUUGG
	3135	GCCAAGCC	CUGAUGA	X	GAA	AAGUCACA	UGUGACUUU	GGCUUGGC
	3140	CCCGGGCC	CUGAUGA	X	GAA	AGCCAAAG	CUUUGGCUU	GGCCCGGG
	3151	AAAUAUUU	CUGAUGA	X	GAA	AUCCCGGG	CCCGGGAUA	AAAUAUU
30	3153	UCUUUAUA	CUGAUGA	X	GAA	AUAUCCCG	CGGGAUAUU	UAUAAAGA
	3154	AUCUUUAU	CUGAUGA	X	GAA	AAUAUCCC	GGGAUAUUU	AUAAAGAU
	3155	GAUCUUUA	CUGAUGA	X	GAA	AAAUAUCC	GGAUAUUUA	UAAAGAUC
	3157	UGGAUCUU	CUGAUGA	X	GAA	AUAAAUAU	AUAUUUAUA	AAGAUCCA

	3163	AUAAUCUG	CUGAUGA	x	GAA	AUCUUUAU	AUAAAGAUC	CAGAUUAU
	3169	UCUGACAU	CUGAUGA	X	GAA	AUCUGGAU	AUCCAGAUU	AUGUCAGA
	3170	UUCUGACA	CUGAUGA	x	GAA	AAUCUGGA	UCCAGAUUA	UGUCAGAA
	3174	ccuuuucu	CUGAUGA	x	GAA	ACAUAAUC	GAUUAUGUC	AGAAAAGG
5	3190	AGGGAGGC	CUGAUGA	X	GAA	AGCAUCUC	GAGAUGCUC	GCCUCCCU
	3195	UUCAAAGG	CUGAUGA	X	GAA	AGGCGAGC	GCUCGCCUC	CCUUUGAA
	3199	CCAUUUCA	CUGAUGA	X	GAA	AGGGAGGC	GCCUCCCUU	UGAAAUGG
	3200	UCCAUUUC	CUGAUGA	x	GAA	AAGGGAGG	ccucccuuu	GAAAUGGA
	3225	CUGUCAAA	CUGAUGA	x	GAA	AUUGUUUC	GAAACAAUU	UUUGACAG
10	3226	UCUGUCAA	CUGAUGA	X	GAA	AAUUGUUU	AAACAAUUU	UUGACAGA
	3227	CUCUGUCA	CUGAUGA	X	GAA	AAAUUGUU	AACAAUUUU	UGACAGAG
	3228	ACUCUGUC	CUGAUGA	x	GAA	AAAAUUGU	ACAAUUUUU	GACAGAGU
	3239	GGAUUGUG	CUGAUGA	x	GAA	ACACUCUG	CAGAGUGUA	CACAAUCC
	3246	UCACUCUG	CUGAUGA	Х	GAA	AUUGUGUA	UACACAAUC	CAGAGUGA
15	3258	AAAGACCA	CUGAUGA	Х	GAA	ACGUCACU	AGUGACGUC	UGGUCUUU
	3263	CACCAAAA	CUGAUGA	Х	GAA	ACCAGACG	CGUCUGGUC	UUUUGGUG
	3265	AACACCAA	CUGAUGA	X	GAA	AGACCAGA	UCUGGUCUU	UUGGUGUU
	3266	AAACACCA	CUGAUGA	х	GAA	AAGACCAG	CUGGUCUUU	UGGUGUUU
	3267	AAAACACC	CUGAUGA	X	GAA	AAAGACCA	UGGUCUUUU	GGUGUUUU
20	3273	CACAGCAA	CUGAUGA	X	GAA	ACACCAAA	UUUGGUGUU	UUGCUGUG
	3274	CCACAGCA	CUGAUGA	X	GAA	AACACCAA	UUGGUGUUU	UGCUGUGG
	3275	CCCACAGC	CUGAUGA	x	GAA	AAACACCA	UGGUGUUUU	GCUGUGGG
	3288	AAGGAAAA	CUGAUGA	X	GAA	AUUUCCCA	UGGGAAAUA	υυυυςςυυ
	3290	CUAAGGAA	CUGAUGA	x	GAA	AUAUUUCC	GGAAAUAUU	UUCCUUAG
25	3291	CCUAAGGA	CUGAUGA	x	GAA	AAUAUUUC	GAAAUAUUU	UCCUUAGG
	3292	ACCUAAGG	CUGAUGA	X	GAA	UUUAUAAA	UUUUAUAAA	CCUUAGGU
	3293	CACCUAAG	CUGAUGA	x	GAA	UUAUAAAA	AAUAUUUUC	CUUAGGUG
	3296	AAGCACCU	CUGAUGA	X	GAA	AGGAAAAU	AUUUUCCUU	AGGUGCUU
	3297	GAAGCACC	CUGAUGA	x	GAA	AAGGAAAA	UUUUCCUUA	GGUGCUUC
30	3304	AUAUGGAG	CUGAUGA	x	GAA	AGCACCUA	UAGGUGCUU	CUCCAUAU
	3305	GAUAUGGA	CUGAUGA	X	GAA	AAGCACCU	AGGUGCUUC	UCCAUAUC
	3307	AGGAUAUG	CUGAUGA	x	GAA	AGAAGCAC	GUGCUUCUC	CAUAUCCU
	3311	CCCCAGGA	CUGAUGA	X	GAA	AUGGAGAA	UUCUCCAUA	UCCUGGGG

	3313	UACCCCAG	CUGAUGA	Х	GAA	AUAUGGAG	CUCCAUAU	CUGGGGUA
	3321	UCAAUCUU	CUGAUGA	X	GAA	ACCCCAGG	CCUGGGGU	AAGAUUGA
	3327	UCUUCAUC	CUGAUGA	. X	GAA	AUCUUUAC	GUAAAGAUL	J GAUGAAGA
	3338	GCCUACAA	CUGAUGA	. X	GAA	AUUCUUCA	UGAAGAAUU	UUGUAGGC
5	3339	CGCCUACA	CUGAUGA	. X	GAA	AAUUCUUC	GAAGAAUUU	UGUAGGCG
	3340	UCGCCUAC	CUGAUGA	X	GAA	AAAUUCUU	AAGAAUUUU	GUAGGCGA
	3343	CAAUCGCC	CUGAUGA	X	GAA	ACAAAAUU	AAUUUUGUA	GGCGAUUG
	3350	CUUCUUUC	CUGAUGA	X	GAA	AUCGCCUA	UAGGCGAUU	GAAAGAAG
	3364	CCUCAUUC	CUGAUGA	X	GAA	AGUUCCUU	AAGGAACUA	GAAUGAGG
.10	3382	UGUAGUAU	CUGAUGA	X	GAA	AUCAGGGG	CCCCUGAUU	AUACUACA
	3383	GUGUAGUA	CUGAUGA	X	GAA	AAUCAGGG	CCCUGAUUA	UACUACAC
	3385	ÜGGUGUAG	CUGAUGA	X	GAA	AUAAUCAG	CUGAUUAUA	CUACACCA
	3388	UUCUGGUG	CUGAUGA	X	GAA	AGUAUAAU	AUUAUACUA	CACCAGAA
	3401	UGGUCUGG	CUGAUGA	X	GAA	ACAUUUCU	AGAAAUGUA	CCAGACCA
15	3439	GGGUCUCU	CUGAUGA	X	GAA	ACUGGGCU	AGCCCAGUC	AGAGACCC
	3452	ACUCUGAA	CUGAUGA	X	GAA	ACGUGGGU	ACCCACGUU	UUCAGAGU
	3453	AACUCUGA	CUGAUGA	X	GAA	AACGUGGG	CCCACGUUU	UCAGAGUU
	3454	CAACUCUG	CUGAUGA	X	GAA	AAACGUGG	CCACGUUUU	CAGAGUUG
	3455	CCAACUCU	CUGAUGA	X	GAA	AAAACGUG	CACGUUUUC	AGAGUUGG
20	3461	GUUCCACC	CUGAUGA	X	GAA	ACUCUGAA	UUCAGAGUU	GGUGGAAC
	3472	AUUUCCCA	CUGAUGA	X	GAA	AUGUUCCA	UGGAACAUU	UGGGAAAU
	3473	GAUUUCCC	CUGAUGA	X	GAA	AAUGUUCC	GGAACAUUU	GGGAAAUC
	3481	UUGCAAGA	CUGAUGA	X	GAA	AUUUCCCA	UGGGAAAUC	UCUUGCAA
	3483	GCUUGCAA	CUGAUGA	X	GAA	AGAUUUCC	GGAAAUCUC	UUGCAAGC
25	3485	UAGCUUGC	CUGAUGA	X	GAA	AGAGAUUU	AAAUCUCUU	GCAAGCUA
	3493	CUGAGCAU	CUGAUGA	X	GAA	AGCUUGCA	UGCAAGCUA	AUGCUCAG
	3499	AUCCUGCU	CUGAUGA	X	GAA	AGCAUUAG	CUAAUGCUC	AGCAGGAU
	3518	GAACAAUG	CUGAUGA	X	GAA	AGUCUUUG	CAAAGACUA	CAUUGUUC
	3522	GGAAGAAC	CUGAUGA	X	GAA	AUGUAGUC	GACUACAUU	GUUCUUCC
30	3525	AUCGGAAG	CUGAUGA	X	GAA	ACAAUGUA	UACAUUGUU	CUUCCGAU
	3526	UAUCGGAA	CUGAUGA	X	GAA	AACAAUGU	ACAUUGUUC	UUCCGAUA
	3528	GAUAUCGG	CUGAUGA	X	GAA	AGAACAAU	AUUGUUCUU	CCGAUAUC
	3529	UGAUAUCG	CUGAUGA	X	GAA	AAGAACAA	UUGUUCUUC	CGAUAUCA

	3534	GUCUCUGA	CUGAUGA	х	GAA	AUCGGAAG	CUUCCGAUA	UCAGAGAC
	3536	AAGUCUCU	CUGAUGA	X	GAA	AUAUCGGA	UCCGAUAUC	AGAGACUU
	3544	CAUGCUCA	CUGAUGA	X	GAA	AGUCUCUG	CAGAGACUU	UGAGCAUG
	3545	CCAUGCUC	CUGAUGA	X	GAA	AAGUCUCU	AGAGACUUU	GAGCAUGG
5	3562	GAGUCCAG	CUGAUGA	х	GAA	AUCCUCUU	AAGAGGAUU	CUGGACUC
	3563	AGAGUCCA	CUGAUGA	X	GAA	AAUCCUCU	AGAGGAUUC	UGGACUCU
	3570	GGCAGAGA	CUGAUGA	X	GAA	AGUCCAGA	UCUGGACUC	UCUCUGCC
	3572	UAGGCAGA	CUGAUGA	X	GAA	AGAGUCCA	UGGACUCUC	UCUGCCUA
	3574	GGUAGGCA	CUGAUGA	X	GAA	AGAGAGUC	GACUCUCUC	UGCCUACC
10	3580	AGGUGAGG	CUGAUGA	Х	GAA	AGGCAGAG	CUCUGCCUA	CCUCACCU
	3584	AAACAGGU	CUGAUGA	Х	GAA	AGGUAGGC	GCCUACCUC	ACCUGUUU
	3591	AUACAGGA	CUGAUGA	х	GAA	ACAGGUGA	UCACCUGUU	UCCUGUAU
	3592	CAUACAGG	CUGAUGA	X	GAA	AACAGGUG	CACCUGUUU	CCUGUAUG
	3593	CCAUACAG	CUGAUGA	X	GAA	AAACAGGU	ACCUGUUUC	CUGUAUGG
15	3598	CUCCUCCA	CUGAUGA	X	GAA	ACAGGAAA	UUUCCUGUA	UGGAGGAG
	3615	GGGUCACA	CUGAUGA	X	GAA	ACUUCCUC	GAGGAAGUA	UGUGACCC
	3629	CAUAAUGG	CUGAUGA	X	GAA	AUUUGGGG	CCCCAAAUU	CCAUUAUG
	3630	UCAUAAUG	CUGAUGA	X	GAA	AAUUUGGG	CCCAAAUUC	CAUUAUGA
	3634	GUUGUCAU	CUGAUGA	X	GAA	AUGGAAUU	AAUUCCAUU	AUGACAAC
20	3635	UGUUGUCA	CUGAUGA	X	GAA	AAUGGAAU	AUUCCAUUA	UGACAACA
	3654	UACUGACU	CUGAUGA	X	GAA	AUUCCUGC	GCAGGAAUC	AGUCAGUA
	3658	CAGAUACU	CUGAUGA	X	GAA	ACUGAUUC	GAAUCAGUC	AGUAUCUG
	3662	UCUGCAGA	CUGAUGA	X	GAA	ACUGACUG	CAGUCAGUA	UCUGCAGA
	3664	GUUCUGCA	CUGAUGA	X	GAA	AUACUGAC	GUCAGUAUC	UGCAGAAC
25	3676	CUUUCGCU	CUGAUGA	X	GAA	ACUGUUCU	AGAACAGUA	AGCGAAAG
	3702	AAUGUUUU	CUGAUGA	X	GAA	ACACUCAC	GUGAGUGUA	AAAACAUU
	3710	UAUCUUCA	CUGAUGA	X	GAA	AUGUUUUU	AAAAACAUU	UGAAGAUA
	3711	AUAUCUUC	CUGAUGA	X	GAA	AAUGUUUU	AAAACAUUU	GAAGAUAU
	3718	UAACGGGA	CUGAUGA	X	GAA	AUCUUCAA	UUGAAGAUA	UCCCGUUA
30	3720	UCUAACGG	CUGAUGA	X	GAA	AUAUCUUC	GAAGAUAUC	CCGUUAGA
	3725	GUUCUUCU	CUGAUGA	X	GAA	ACGGGAUA	UAUCCCGUU	AGAAGAAC
	3726	GGUUCUUC	CUGAUGA	X	GAA	AACGGGAU	AUCCCGUUA	GAAGAACC
	3741	AUUACUUU	CUGAUGA	X	GAA	ACUUCUGG	CCAGAAGUA	AAAGUAAU

-72

.js:

	3747	UCUGGGAU	CUGAUGA	X	GAA	ACUUUUAC	GUAAAAGUA	AUCCCAGA
	3750	UCAUCUGG	CUGAUGA	. х	GAA	AUUACUUU	AAAGUAAUC	CCAGAUGA
	3778	AAGAACCA	CUGAUGA	. x	GAA	ACCACUGU	ACAGUGGUA	ugguucuu
	3783	GAGGCAAG	CUGAUGA	. x	GAA	ACCAUACC	GGUAUGGUU	CUUGCCUC
5	3784	UGAGGCAA	CUGAUGA	X	GAA	AACCAUAC	GUAUGGUUC	UUGCCUCA
	3786	UCUGAGGC	CUGAUGA	X	GAA	AGAACCAU	AUGGUUCUU	GCCUCAGA
	3791	GCUCUUCU	CUGAUGA	X	GAA	AGGCAAGA	UCUUGCCUC	AGAAGAGC
	3808	GUCUUCCA	CUGAUGA	Х	GAA	AGUUUUCA	UGAAAACUU	UGGAAGAC
	3809	UGUCUUCC	CUGAUGA	X	GAA	AAGUUUUC	GAAAACUUU	GGAAGACA
10	3827	AUGGAGAU	CUGAUGA	X	GAA	AUUUGGUU	AACCAAAUU	AUCUCCAU
	3828	GAUGGAGA	CUGAUGA	X	GAA	AAUUUGGU	ACCAAAUUA	UCUCCAUC
	3830	AAGAUGGA	CUGAUGA	X	GAA	AUAAUUUG	CAAAUUAUC	UCCAUCUU
	3832	AAAAGAUG	CUGAUGA	X	GAA	AGAUAAUU	AAUUAUCUC	CAUCUUUU
	3836	CACCAAAA	CUGAUGA	X	GAA	AUGGAGAU	AUCUCCAUC	UUUUGGUG
15	3838	UCCACCAA	CUGAUGA	X	GAA	AGAUGGAG	CUCCAUCUU	UUGGUGGA
	3839	UUCCACCA	CUGAUGA	x	GAA	AAGAUGGA	UCCAUCUUU	UGGUGGAA
	3840	AUUCCACC	CUGAUGA	X	GAA	AAAGAUGG	CCAUCUUUU	GGUGGAAU
	3872	AUGCCACA	CUGAUGA	x	GAA	ACUCCCUG	CAGGGAGUC	UGUGGCAU
	3881	AGCCUUCA	CUGAUGA	X	GAA	AUGCCACA	UGUGGCAUC	UGAAGĠCU
20	3890	UCUGGUUU	CUGAUGA	X	GAA	AGCCUUCA	UGAAGGCUC	AAACCAGA
	3908	CGGACUGG	CUGAUGA	x	GAA	AGCCGCUU	AAGCGGCUA	CCAGUCCG
	3914	GAUAUCCG	CUGAUGA	x	GAA	ACUGGUAG	CUACCAGUC	CGGAUAUC
	3920	CGGAGUGA	CUGAUGA	X	GAA	AUCCGGAC	GUCCGGAUA	UCACUCCG
	3922	AUCGGAGU	CUGAUGA	x	GAA	AUAUCCGG	CCGGAUAUC	ACUCCGAU
25	3926	UGUCAUCG	CUGAUGA	X	GAA	AGUGAUAU	AUAUCACUC	CGAUGACA
	3950	CACUGGAG	CUGAUGA	X	GAA	ACACGGUG	CACCGUGUA	CUCCAGUG
	3953	CCUCACUG	CUGAUGA	X	GAA	AGUACACG	CGUGUACUC	CAGUGAGG
	3972	AGCUUUAA	CUGAUGA	X	GAA	AGUUCUGC	GCAGAACUU	UUAAAGCU
	3973	CAGCUUUA	CUGAUGA	x	GAA	AAGUUCUG	CAGAACUUU	UAAAGCUG
30	3974	UCAGCUUU	CUGAUGA	X	GAA	AAAGUUCU	AGAACUUUU	AAAGCUGA
	3975	AUCAGCUU	CUGAUGA	X	GAA	AAAAGUUC	GAACUUUUA	AAGCUGAU
	3984	CCAAUCUC	CUGAUGA	x	GAA	AUCAGCUU	AAGCUGAUA	GAGAUUGG
	3990	UGCACUCC	CUGAUGA	X	GAA	AUCUCUAU	AUAGAGAUU	GGAGUGCA

	4006	GGCUGUGC	CUGAUGA	Х	GAA	ACCGGUUU	AAACCGGUA	GCACAGCC
	4020	GGCUGGAG	CUGAUGA	X	GAA	AUCUGGGC	GCCCAGAUU	CUCCAGCC
	4021	AGGCUGGA	CUGAUGA	X	GAA	AAUCUGGG	CCCAGAUUC	UCCAGCCU
	4023	UCAGGCUG	CUGAUGA	X	GAA	AGAAUCUG	CAGAUUCUC	CAGCCUGA
5	4052	CAGGAGGA	CUGAUGA	x	GAA	AGCUCAGU	ACUGAGCUC	UCCUCCUG
	4054	AACAGGAG	CUGAUGA	X	GAA	AGAGCUCA	UGAGCUCUC	cuccuguu
	4057	UUAAACAG	CUGAUGA	X	GAA	AGGAGAGC	GCUCUCCUC	CUGUUUAA
	4062	UCCUUUUA	CUGAUGA	X	GAA	ACAGGAGG	CCUCCUGUU	UAAAAGGA
	4063	υυςςυυυυ	CUGAUGA	X	GAA	AACAGGAG	CUCCUGUUU	AAAAGGAA
10	4064	CUUCCUUU	CUGAUGA	x	GAA	AAACAGGA	UCCUGUUUA	AAAGGAAG
	4076	GGGGUGUG	CUGAUGA	x	GAA	AUGCUUCC	GGAAGCAUC	CACACCCC
	4089	AUGUCCGG	CUGAUGA	x	GAA	AGUUGGGG	CCCCAACUC	CCGGACAU
	4098	UCUCAUGU	CUGAUGA	x	GAA	AUGUCCGG	CCGGACAUC	ACAUGAGA
	4110	UCUGAGCA	CUGAUGA	X	GAA	ACCUCUCA	UGAGAGGUC	UGCUCAGA
15	4115	CAAAAUCU	CUGAUGA	X	GAA	AGCAGACC	GGUCUGCUC	AGAUUUUG
	4120	CACUUCAA	CUGAUGA	X	GAA	AUCUGAGC	GCUCAGAUU	UUGAAGUG
	4121	ACACUUCA	CUGAUGA	X	GAA	AAUCUGAG	CUCAGAUUU	UGAAGUGU
	4122	AACACUUC	CUGAUGA	X	GAA	AAAUCUGA	UCAGAUUUU	GAAGUGUU
	4130	GAAAGAAC	CUGAUGA	X	GAA	ACACUUCA	UGAAGUGUU	GUUCUUUC
20	4133	GUGGAAAG	CUGAUGA	X	GAA	ACAACACU	AGUGUUGUU	CUUUCCAC
	4134	GGUGGAAA	CUGAUGA	x	GAA	AACAACAC	GUGUUGUUC	UUUCCACC
	4136	CUGGUGGA	CUGAUGA	x	GAA	AGAACAAC	GUUGUUCUU	UCCACCAG
	4137	GCUGGUGG	CUGAUGA	x	GAA	AAGAACAA	UUGUUCUUU	CCACCAGC
	4138	UGCUGGUG	CUGAUGA	X	GAA	AAAGAACA	UGUUCUUUC	CACCAGCA
25	4153	AAUGCGGC	CUGAUGA	x	GAA	ACUUCCUG	CAGGAAGUA	GCCGCAUU
	4161	GAAAAUCA	CUGAUGA	X	GAA	AUGCGGCU	AGCCGCAUU	UGAUUUUC
	4162	UGAAAAUC	CUGAUGA	X	GAA	AAUGCGGC	GCCGCAUUU	GAUUUUCA
	4166	GAAAUGAA	CUGAUGA	x	GAA	AUCAAAUG	CAUUUGAUU	UUCAUUUC
	4167	CGAAAUGA	CUGAUGA	x	GAA	AAUCAAAU	AUUUGAUUU	UCAUUUCG
30	4168	UCGAAAUG	CUGAUGA	X	GAA	AAAUCAAA	UUUGAUUUU	CAUUUCGA
	4169	GUCGAAAU	CUGAUGA	x	GAA	AAAAUCAA	UUGAUUUUC	AUUUCGAC
	4172	GUUGUCGA	CUGAUGA	X	GAA	AUGAAAAU	AUUUUCAUU	UCGACAAC
	4173	UGUUGUCG	CUGAUGA	x	GAA	AAUGAAAA	UUUUCAUUU	CGACAACA

117

	4174	cuguuguc	CUGAUGA	Х	GAA	AAAUGAAA	UUUCAUUUC	GACAACAG
	4194	UGCAGUCC	CUGAUGA	X	GAA	AGGUCCUU	AAGGACCUC	GGACUGCA
	4214	GCCUAGAA	CUGAUGA	X	GAA	AGCUGGCU	AGCCAGCUC	UUCUAGGC
	4216	AAGCCUAG	CUGAUGA	X	GAA	AGAGCUGG	CCAGCUCUU	CUAGGCUU
5	4217	CAAGCCUA	CUGAUGA	X	GAA	AAGAGCUG	CAGCUCUUC	UAGGCUUG
	4219	CACAAGCC	CUGAUGA	х	GAA	AGAAGAGC	GCUCUUCUA	GGCUUGUG

Where "X" represents stem II region of a HH ribozyme (Hertel et al., 1992 $Nucleic\ Acids\ Res$. 20 3252). The length of stem II may be \ge 2 base-pairs.

11

Table V: Human KDR VEGF Receptor-Hairpin Ribozyme and Substrate Sequences

	nt.	Hairpin Ribozyme Sequence	Substrate
	Position	r.	
	11	CGACGGCC AGAA GCACCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	AGGUGCU GCU GGCCGUCG
Ŋ	18	CACAGGGC AGAA GCCAGC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	ecneecc enc eccanene
	51	CCCACAGA AGAA GCCCGG ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	aceeecc ecc naneneee
	86	UGAGCCUG AGAA GAUCAA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UNGAUCU GCC CAGGCUCA
	318	GAGGCCAA AGAA GUUUCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	GGAAACU GAC UUGGCCUC
	358	AAAUGGAG AGAA GUAAUC ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	GAUUACA GAU CUCCAUUU
10	510	CUGUUACC AGAA GGAACA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UGUUCCU GAU GGUAACAG
	623	ACAUAAUA AGAA GGUAAC ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	GUUACCA GUC UAUUAUGU
	683	UUCCAUGA AGAA GACUCA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UGAGUCC GUC UCAUGGAA
	705	UUUUCUCC AGAA GAUAGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	ACUAUCU GUU GGAGAAAA
	833	CACUCCCA AGAA GGGUUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	AAACCCA GUC UGGGAGUG
15	932	UCUUGGUC AGAA GCCCAC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	GUGGGCU GAU GACCAAGA
	1142	CCAUAAUC AGAA GUACAU ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	AUGUACU GAC GAUUAUGG
	1259	UCUCACCA AGAA GGGGUG ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CACCCCA GAU UGGUGAGA
	1332	AUGGCAUA AGAA GUACAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	AUGUACG GUC UAUGCCAU

GCU CUGGAUUU

UCAGCCA

ACUUCCU GAC CUUGGAGC

GGAAGU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA

GCUCCAAG AGAA

2993

15

GGCUGA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA

119 AUUGGCA GUU GGAGGAAG CCAAGCU GUC UCAGUGAC UGUGUCA, GCU UUGUACAA ACAUGCA GCC CACUGAGC GCCCACA GCC UCUGCCAA CACACCU GUU UGCAAGAA GAU CUACGUUU UAUGUCU GCC UUGCUCAA GCU CACAGUCC CUAGAGCG AACGACU GCC UUAUGAUG GAGACCG GCU GAACCUAG AGAAUCA GAC GACAAGUA CUCCACA GAU CAUGUGGU GAU GAACUCCC GCCUNNGG CACUUACC GCUCACA GUC GAU GNC GCAGACA UCAGGCA GGAUCCA GAAACCU UGAAGCA CUUCCUCC AGAA GCCAAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUCACUGA AGAA GCUUGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GACACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCAUGU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GUCUGC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GUGGGC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA UUCUUGCA AGAA GGUGUG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UUGAGCAA AGAA GACAUA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA GCCUGA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CGCUCUAG AGAA GUGAGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UACUUGUC AGAA GAUUCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUGGAG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CAUCAUAA AGAA GUCGUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGUCUC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGGAGUUC AGAA GGAUCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CCAAAGGC AGAA GCUUCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGUAAGUG AGAA GGUUUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UUGUACAA AGAA SCUCAGUG AGAA AAACGUAG AGAA AGAA SGACUGUG AGAA ACCACAUG AGAA CUAGGUUC AGAA AAAUCCAG AGAA UUGGCAGA 1413 1569 1673 1717 1760 1918 1797 2418 1967 1974 2084 2453 2492 2547 2765 2021 2914

10

119

1376

ഗ

GACCUCG GAC UGCAGGGA

UCCCUGCA AGAA GAGGUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

	120																
UGUUACA GCU UCCAAGUG	AGAUCCA GAU UAUGUCAG	GGCCCCU GAU NAUACUAC	UGUACCA GAC CAUGCUGG	CUGGACU GCU GGCACGGG	ucucucu gcc uaccucac	CUCACCU GUU UCCUGUAU	AGAGCCG GCC UGUGAGUG	AAUCCCA GAU GACAACCA	ACAACCA GAC GGACAGUG	GCUACCA GUC CGGAUAUC	UCACUCC GAU GACACAGA	UAGCACA GCC CAGAUUCU	CAGCCCA GAU UCUCCAGC	UUCUCCA GCC UGACACGG	UCCUCCU GUU UAAAAGGA	GAGGUCU GCU CAGAUUUU	CUGCUCA GAU UUUGAAGU
CACUUGGA AGAA GUAACA ACCAGAGAAACACGCUGGUGGUACAUUACCUGGUA	CUGACAUA AGAA GGAUCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GUAGUAUA AGAA GGGGCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CCAGCAUG AGAA GGUACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CCCGUGCC AGAA GUCCAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GUGAGGUA AGAA GAGAGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	AUACAGGA AGAA GGUGAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CACUCACA AGAA GGCUCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UGGUUGUC AGAA GGGAUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CACUGUCC AGAA GGUUGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GAUAUCCG AGAA GGUAGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UCUGUGUC AGAA GAGUGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	AGAAUCUG AGAA GUGCUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GCUGGAGA AGAA GGGCUG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CCGUGUCA AGAA GGAGAA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UCCUUUUA AGAA GGAGGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	AAAAUCUG AGAA GACCUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	ACUUCAAA AGAA GAGCAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA
3019	3165	3378	3404	3418	3575	3588	3689	3753	3764	3911	3927	4011	4016	4025	4059	4111	4116

GGAGCCA GCU CUUCUAGG

CCUAGAAG AGAA GGCUCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

121

122

Table VI: Mouse flk-1 VEGF Receptor-Hammerhead Ribozyme and Substrate Sequence

	nt. Posi				Sequ	ence	Substrate		
5	tion			٠					
	13	CCGUACCC	CUGAUGA	х	GAA	AUUCGCCC	GGGCGAAUU	GGGUACGG	
	18	GGGUCCCG	CUGAUGA	X	GAA	ACCCAAUU	AAUUGGGUA	CGGGACCC	
	31	UCGACCUC	CUGAUGA	Х	GAA	AGGGGGGU	ACCCCCCUC	GAGGUCGA	
	37	AUACCGUC	CUGAUGA	Х	GAA	ACCUCGAG	CUCGAGGUC	GACGGUAU	
10	44	CUUAUCGA	CUGAUGA	х	GAA	ACCGUCGA	UCGACGGUA	UCGAUAAG	
	46	AGCUUAUC	CUGAUGA	X	GAA	AUACCGUC	GACGGUAUC	GAUAAGCU	
	50	AUCAAGCU	CUGAUGA	X	GAA	AUCGAUAC	GUAUCGAUA	AGCUUGAU	
	55	UCGAUAUC	CUGAUGA	x	GAA	AGCUUAUC	GAUAAGCUU	GAUAUCGA	
	59	GAAUUCGA	CUGAUGA	X	GAA	AUCAAGCU	AGCUUGAUA	UCGAAUUC	
15	61	CCGAAUUC	CUGAUGA	X	GAA	AUAUCAAG	CUUGAUAUC	GAAUUCGG	
	6 6	UGGGCCCG	CUGAUGA	X	GAA	AUUCGAUA	UAUCGAAUU	CGGGCCCA	
	67	CUGGGCCC	CUGAUGA	х	GAA	AAUUCGAU	AUCGAAUUC	GGGCCCAG	
	83	GGCUGCGG	CUGAUGA	X	GAA	ACACAGUC	GACUGUGUC	CCGCAGCC	
	97	AGCCAGGU	CUGAUGA	X	GAA	AUCCCGGC	GCCGGGAUA	ACCUGGCU	
20	114	GUCCGCGG	CUGAUGA	X	GAA	AUCGGGUC	GACCCGAUU	CCGCGGAC	
	115	UGUCCGCG	CUGAUGA	x	GAA	AAUCGGGU	ACCCGAUUC	CGCGGACA	
	169	ACCGGGGA	CUGAUGA	X	GAA	AGCGCGGG	CCCGCGCUC	UCCCCGGU	
	171	AGACCGGG	CUGAUGA	x	GAA	AGAGCGCG	CGCGCUCUC	CCCGGUCU	
	178	CAGCGCAA	CUGAUGA	X	GAA	ACCGGGGA	UCCCCGGUC	UUGCGCUG	
25	180	CGCAGCGC	CUGAUGA	X	GAA	AGACCGGG	CCCGGUCUU	GCGCUGCG	
	197	AGAGGCGG	CUGAUGA	Х	GAA	AUGGCCCC	GGGGCCAUA	ccgccucu	
	204	AAGUCACA	CUGAUGA	X	GAA	AGGCGGUA	UACCGCCUC	UGUGACUU	
	212	CCGCAAAG	CUGAUGA	X	GAA	AGUCACAG	CUGUGACUU	CUUUGCGG	
	213	CCCGCAAA	CUGAUGA	Х	GAA	AAGUCACA	UGUGACUUC	UUUGCGGG	
30	215	GGCCCGCA	CUGAUGA	х	GAA	AGAAGUCA	UGACUUCUU	UGCGGGCC	

*

**

Ž.

	216	UGGCCCG	C CUGAUGA	A 2	K GA	A AAGAAGUC	GACUUCUUU	GCGGGCCA
	241	CAGGCAC	A CUGAUGA	A 3	GA/	A ACUCCUUC	GAAGGAGUC	UGUGCCUG
	262	UGGGCACA	A CUGAUGA	A >	(GA	A AGCCCAGU	ACUGGGCUC	UGUGCCCA
	306	GCGACAG	CUGAUGA	λ >	GA/	A AGCAGCGC	GCGCUGCUA	GCUGUCGC
5	312	CACAGAG	C CUGAUGA	λ λ	GAA	A ACAGCUAG	CUAGCUGUC	GCUCUGUG
	316	GAACCACA	A CUGAUGA	X	GA.	AGCGACAG	CUGUCGCUC	UGUGGUUC
	323	CCACGCAC	G CUGAUGA	X	GAA	ACCACAGA	UCUGUGGUU	CUGCGUGG
	324	UCCACGCA	CUGAUGA	Х	GAA	AACCACAG	CUGUGGUUC	UGCGUGGA
	347	AACCCACA	CUGAUGA	. X	GAA	AGGCGGCU	AGCCGCCUC	UGUGGGUU
10	355	GCCAGUCA	CUGAUGA	. X	GAA	ACCCACAG	CUGUGGGUU	UGACUGGC
	356	CGCCAGUC	CUGAUGA	X	GAA	AACCCACA	UGUGGGUUU	GACUGGCG
	367	AUGGAGAA	CUGAUGA	X	GAA	AUCGCCAG	CUGGCGAUU	UUCUCCAU
	3 6 8	GAUGGAGA	CUGAUGA	X	GAA	AAUCGCCA	UGGCGAUUU	UCUCCAUC
	369	GGAUGGAG	CUGAUGA	Х	GAA	AAAUCGCC	GGCGAUUUU	CUCCAUCC
15	370	GGGAUGGA	CUGAUGA	X	GAA	AAAAUCGC	GCGAUUUUC	UCCAUCCC
	372	GGGGGAUG	CUGAUGA	Х	GAA	AGAAAAUC	GAUUUUCUC	CAUCCCCC
	376	CUUGGGGG	CUGAUGA	Х	GAA	AUGGAGAA	UUCUCCAUC	CCCCCAAG
	387	UGUGUGCU	CUGAUGA	Х	GAA	AGCUUGGG	CCCAAGCUC	AGCACACA
	405	AUUGUCAG	CUGAUGA	Х	GAA	AUGUCUUU	AAAGACAUA	CUGACAAU
20	414	UUUGCCAA	CUGAUGA	X	GAA	AUUGUCAG	CUGACAAUU	UUGGCAAA
	415	AUUUGCCA	CUGAUGA	X	GAA	AAUUGUCA	UGACAAUUU	UGGCAAAU
	416	UAUUUGCC	CUGAUGA	X	GAA	AAAUUGUC	GACAAUUUU (GGCAAAUA
	424	AAGGGUUG	CUGAUGA	X	GAA	AUUUGCCA	UGGCAAAUA (CAACCCUU
	432	GUAAUCUG	CUGAUGA	Х	GAA	AGGGUUGU	ACAACCCUU (CAGAUUAC
25	433	AGUAAUCU	CUGAUGA	X	GAA	AAGGGUUG	CAACCCUUC A	AGAUUACU
	438	CUGCAAGU	CUGAUGA	x	GAA	AUCUGAAG	CUUCAGAUU A	ACUUGCAG
	439	CCUGCAAG	CUGAUGA	X	GAA	AAUCUGAA	UUCAGAUUA (JUUGCAGG
	442	UCCCCUGC	CUGAUGA	X	GAA	AGUAAUCU	AGAUUACUU C	CAGGGGA
	471	UUGGGCCA	CUGAUGA	X	GAA	AGCCAGUC	GACUGGCUU L	JGGCCCAA
30	472	AUUGGGCC	CUGAUGA	X	GAA	AAGCCAGU	ACUGGCUUU G	GCCCAAU

WO 97/15662

	484	AUCACGCU	CUGAUGA	X	GAA	AGCAUUGG	CCAAUGCUC	AGCGUGAU
	493	UUCCUCAG	CUGAUGA	x	GAA	AUCACGCU	AGCGUGAUU	CUGAGGAA
	494	UUUCCUCA	CUGAUGA	Х	GAA	AAUCACGC	GCGUGAUUC	UGAGGAAA
	507	GUCACCAA	CUGAUGA	х	GAA	ACCCUUUC	GAAAGGGUA	UUGGUGAC
5	509	CAGUCACC	CUGAUGA	х	GAA	AUACCCUU	AAGGGUAUU	GGUGACUG
	538	GCAGAAGA	CUGAUGA	x	GAA	ACUGUCAC	GUGACAGUA	UCUUCUGC
	54 0	UUGCAGAA	CUGAUGA	х	GAA	AUACUGUC	GACAGUAUC	UUCUGCAA
	542	UUUUGCAG	CUGAUGA	Х	GAA	AGAUACUG	CAGUAUCUU	CUGCAAAA
	543	GUUUUGCA	CUGAUGA	х	GAA	AAGAUACU	AGUAUCUUC	UGCAAAAC
10	555	GGAAUGGU	CUGAUGA	х	GAA	AGUGUUUU	AAAACACUC	ACCAUUCC
	561	ACCCUGGG	CUGAUGA	Х	GAA	AUGGUGAG	CUCACCAUU	CCCAGGGU
	56 2	CACCCUGG	CUGAUGA	X	GAA	AAUGGUGA	UCACCAUUC	CCAGGGUG
	57 3	UCAUUUCC	CUGAUGA	X	GAA	ACCACCCU	AGGGUGGUU	GGAAAUGA
	583	GGCUCCAG	CUGAUGA	Х	GAA	AUCAUUUC	GAAAUGAUA	CUGGAGCC
15	59 3	AGCACUUG	CUGAUGA	X	GAA	AGGCUCCA	UGGAGCCUA	CAAGUGCU
	602	CCCGGUAC	CUGAUGA	Х	GAA	AGCACUUG	CAAGUGCUC	GUACCGGG
	605	CGUCCCGG	CUGAUGA	Х	GAA	ACGAGCAC	GUGCUCGUA	CCGGGACG
	615	GCUAUGUC	CUGAUGA	х	GAA	ACGUCCCG	CGGGACGUC	GACAUAGC
	621	GUGGAGGC	CUGAUGA	х	GAA	AUGUCGAC	GUCGACAUA	GCCUCCAC
20	626	AAACAGUG	CUGAUGA	Х	GAA	AGGCUAUG	CAUAGCCUC	CACUGUUU
	633	UAGACAUA	CUGAUGA	x	GAA	ACAGUGGA	UCCACUGUU	UAUGUCUA
	634	AUAGACAU	CUGAUGA	х	GAA	AACAGUGG	CCACUGUUU	AUGUCUAU
	63 5	CAUAGACA	CUGAUGA	х	GAA	AAACAGUG	CACUGUUUA	UGUCUAUG
	639	CGAACAUA	CUGAUGA	x	GAA	ACAUAAAC	GUUUAUGUC	UAUGUUCG
25	641	CUCGAACA	CUGAUGA	х	GAA	AGACAUAA	UUAUGUCUA	UGUUCGAG
	645	UAAUCUCG	CUGAUGA	x	GAA	ACAUAGAC	GUCUAUGUU	CGAGAUUA
	646	GUAAUCUC	CUGAUGA	х	GAA	AACAUAGA	UCUAUGUUC	GAGAUUAC
	652	UGAUCUGU	CUGAUGA	X	GAA	AUCUCGAA	UUCGAGAUU	ACAGAUCA
	65 3	GUGAUCUG	CUGAUGA	X	GAA	AAUCUCGA	UCGAGAUUA	CAGAUCAC
30	659	UGAAUGGU	CUGAUGA	X	GAA	AUCUGUAA	UUACAGAUC	ACCAUUCA

	665	AGGCGAUG CUGAUGA X GAA AUGGUGAU AUCACCAUU CAUCGCCU
	666	GAGGCGAU CUGAUGA X GAA AAUGGUGA UCACCAUUC AUCGCCUC
	6 69	ACAGAGGC CUGAUGA X GAA AUGAAUGG CCAUUCAUC GCCUCUGU
	674	CACUGACA CUGAUGA X GAA AGGCGAUG CAUCGCCUC UGUCAGUG
5	678	UGGUCACU CUGAUGA X GAA ACAGAGGC GCCUCUGUC AGUGACCA
	69 6	AUGUACAC CUGAUGA X GAA AUGCCAUG CAUGGCAUC GUGUACAU
	701	CGGUGAUG CUGAUGA X GAA ACACGAUG CAUCGUGUA CAUCACCG
	70 5	UUCUCGGU CUGAUGA X GAA AUGUACAC GUGUACAUC ACCGAGAA
	73 5	CGGCAGGG CUGAUGA X GAA AUCACCAC GUGGUGAUC CCCUGCCG
10	74 9	UUGAAAUC CUGAUGA X GAA ACCCUCGG CCGAGGGUC GAUUUCAA
	75 3	AGGUUUGA CUGAUGA X GAA AUCGACCC GGGUCGAUU UCAAACCU
	754	GAGGUUUG CUGAUGA X GAA AAUCGACC GGUCGAUUU CAAACCUC
	75 5	UGAGGUUU CUGAUGA X GAA AAAUCGAC GUCGAUUUC AAACCUCA
	762	GACACAUU CUGAUGA X GAA AGGUUUGA UCAAACCUC AAUGUGUC
15	77 0	CGCAAAGA CUGAUGA X GAA ACACAUUG CAAUGUGUC UCUUUGCG
	7 72	AGCGCAAA CUGAUGA X GAA AGACACAU AUGUGUCUC UUUGCGCU
	774	CUAGCGCA CUGAUGA X GAA AGAGACAC GUGUCUCUU UGCGCUAG
	7 75	CCUAGCGC CUGAUGA X GAA AAGAGACA UGUCUCUUU GCGCUAGG
	781	UGGAUACC CUGAUGA X GAA AGCGCAAA UUUGCGCUA GGUAUCCA
20	78 5	UUUCUGGA CUGAUGA X GAA ACCUAGCG CGCUAGGUA UCCAGAAA
	787	CUUUUCUG CUGAUGA X GAA AUACCUAG CUAGGUAUC CAGAAAAG
	80 0	CCGGAACA CUGAUGA X GAA AUCUCUUU AAAGAGAUU UGUUCCGG
	801	UCCGGAAC CUGAUGA X GAA AAUCUCUU AAGAGAUUU GUUCCGGA
	804	CCAUCCGG CUGAUGA X GAA ACAAAUCU AGAUUUGUU CCGGAUGG
25	805	UCCAUCCG CUGAUGA X GAA AACAAAUC GAUUUGUUC CGGAUGGA
	822	UCCCAGGA CUGAUGA X GAA AUUCUGUU AACAGAAUU UCCUGGGA
	823	GUCCCAGG CUGAUGA X GAA AAUUCUGU ACAGAAUUU CCUGGGAC
	824	UGUCCCAG CUGAUGA X GAA AAAUUCUG CAGAAUUUC CUGGGACA
	840	GUAAAGCC CUGAUGA X GAA AUCUCGCU AGCGAGAUA GGCUUUAC
30	845	GGAGAGUA CUGAUGA X GAA AGCCUAUC GAUAGGCUU UACUCUCC

	846	GGGAGAGU	CUGAUGA	X	GAA	AAGCCUAU	AUAGGCUUU	ACUCUCCC
	847	GGGGAGAG	CUGAUGA	X	GAA	AAAGCCUA	UAGGCUUUA	CUCUCCCC
	850	ACUGGGGA	CUGAUGA	X	GAA	AGUAAAGC	GCUUUACUC	UCCCCAGU
	852	UAACUGGG	CUGAUGA	X	GAA	AGAGUAAA	UUUACUCUC	CCCAGUUA
5	859	GAUCAUGU	CUGAUGA	Х	GAA	ACUGGGGA	UCCCCAGUU	ACAUGAUC
	860	UGAUCAUG	CUGAUGA	Х	GAA	AACUGGGG	CCCCAGUUA	CAUGAUCA
	867	GCAUAGCU	CUGAUGA	Х	GAA	AUCAUGUA	UACAUGAUC	AGCUAUGC
	872	UGCCGGCA	CUGAUGA	Х	GAA	AGCUGAUC	GAUCAGCUA	UGCCGGCA
	885	UCACAGAA	CUGAUGA	Х	GAA	ACCAUGCC	GGCAUGGUC	UUCUGUGA
10	887	CCUCACAG	CUGAUGA	Х	GAA	AGACCAUG	CAUGGUCUU	CUGUGAGG
	888	GCCUCACA	CUGAUGA	X	GAA	AAGACCAU	AUGGUCUUC	UGUGAGGC
	903	UCAUCAUU	CUGAUGA	X	GAA	AUCUUUGC	GCAAAGAUC	AAUGAUGA
	917	UAGACUGA	CUGAUGA	Х	GAA	AGGUUUCA	UGAAACCUA	UCAGUCUA
	919	GAUAGACU	CUGAUGA	X	GAA	AUAGGUUU	AAACCUAUC	AGUCUAUC
15	923	ACAUGAUA	CUGAUGA	Χ	GAA	ACUGAUAG	CUAUCAGUC	UAUCAUGU
	925	GUACAUGA	CUGAUGA	Х	GAA	AGACUGAU	AUCAGUCUA	UCAUGUAC
	927	AUGUACAU	CUGAUGA	X	GAA	AUAGACUG	CAGUCUAUC	AUGUACAU
	932	CAACUAUG	CUGAUGA	Х	GAA	ACAUGAUA	UAUCAUGUA	CAUAGUUG
	936	ACCACAAC	CUGAUGA	Х	GAA	AUGUACAU	AUGUACAUA	GUUGUGGU
20	939	ACAACCAC	CUGAUGA	X	GAA	ACUAUGUA	UACAUAGUU	GUGGUUGU
	945	UAUCCUAC	CUGAUGA	Х	GAA	ACCACAAC	GUUGUGGUU	GUAGGAUA
	948	CUAUAUCC	CUGAUGA	X	GAA	ACAACCAC	GUGGUUGUA	GGAUAUAG
	953	AAAUCCUA	CUGAUGA	X	GAA	AUCCUACA	UGUAGGAUA	UAGGAUUU
	955	AUAAAUCC	CUGAUGA	X	GAA	AUAUCCUA	UAGGAUAUA	GGAUUUAU
2 5	960	ACAUCAUA	CUGAUGA	Х	GAA	AUCCUAUA	UAUAGGAUU	UAUGAUGU
	961	CACAUCAU	CUGAUGA	X	GAA	AAUCCUAU	AUAGGAUUU	AUGAUGUG
	962	UCACAUCA	CUGAUGA	X	GAA	AAAUCCUA	UAGGAUUUA	UGAUGUGA
	97 2	GGGCUCAG	CUGAUGA	X	GAA	AUCACAUC	GAUGUGAUU	CUGAGCCC
	97 3	GGGGCUCA	CUGAUGA	X	GAA	AAUCACAU	AUGUGAUUC	UGAGCCCC
30	993	GAUAGCUC	CUGAUGA	X	GAA	AUUUCAUG	CAUGAAAUU	GAGCUAUC

	99 9	CCGGCAG.	A CUGAUG	A :	X GA	A AGCUCAAU	AUUGAGCUA UCUGCCGG
	100	1 CUCCGGC.	A CUGAUGA	A 2	X GA	A AUAGCUCA	UGAGCUAUC UGCCGGAG
	101	7 UUUAAGA	C CUGAUG	A 2	X GA	A AGUUUUUC	GAAAAACUU GUCUUAAA
	102	O CAAUUUA	A CUGAUGA	A)	K GAZ	A ACAAGUUU	AAACUUGUC UUAAAUUG
5	1022	2 UACAAUUI	J CUGAUGA	A >	(GA	A AGACAAGU	ACUUGUCUU AAAUUGUA
	1023	GUACAAUT	J CUGAUGA	Α >	GA/	A AAGACAAG	CUUGUCUUA AAUUGUAC
	1027	7 CGCUGUA	CUGAUGA	A >	GA,	A AUUUAAGA	UCUUAAAUU GUACAGCG
	1030	UCUCGCU	G CUGAUGA	X	GA,	A ACAAUUUA	UAAAUUGUA CAGCGAGA
	1047	7 CCCACAU	J CUGAUGA	X	GAA	A AGCUCUGU	ACAGAGCUC AAUGUGGG
10	1059	GUGAAAU	CUGAUGA	X	GAA	AGCCCCAC	GUGGGGCUU GAUUUCAC
	1063	CCAGGUGA	CUGAUGA	X	GAA	AUCAAGCC	GGCUUGAUU UCACCUGG
	1064	GCCAGGUG	CUGAUGA	X	GAA	AAUCAAGC	GCUUGAUUU CACCUGGC
	1065	UGCCAGGU	CUGAUGA	. X	GAA	AAAUCAAG	CUUGAUUUC ACCUGGCA
	1076	AAGGUGGA	CUGAUGA	X	GAA	AGUGCCAG	CUGGCACUC UCCACCUU
15	1078	UGAAGGUG	CUGAUGA	X	GAA	AGAGUGCC	GGCACUCUC CACCUUCA
	1084	AGACUUUG	CUGAUGA	X	GAA	AGGUGGAG	CUCCACCUU CAAAGUCU
	1085	GAGACUUU	CUGAUGA	X	GAA	AAGGUGGA	UCCACCUUC AAAGUCUC
	1091	UAUGAUGA	CUGAUGA	X	GAA	ACUUUGAA	UUCAAAGUC UCAUCAUA
	1093	CUUAUGAU	CUGAUGA	Х	GAA	AGACUUUG	CAAAGUCUC AUCAUAAG
20	1096	CUUCUUAU	CUGAUGA	Х	GAA	AUGAGACU	AGUCUCAUC AUAAGAAG
	1099	AAUCUUCU	CUGAUGA	x	GAA	AUGAUGAG	CUCAUCAUA AGAAGAUU
	1107	CGGUUUAC	CUGAUGA	Х	GAA	AUCUUCUU	AAGAAGAUU GUAAACCG
	1110	UCCCGGUU	CUGAUGA	Х	GAA	ACAAUCUU	AAGAUUGUA AACCGGGA
	1130	UCCCAGGA	CUGAUGA	x	GAA	AGGGUUUC	GAAACCCUU UCCUGGGA
2 5	1131	GUCCCAGG	CUGAUGA	Х	GAA	AAGGGUUU	AAACCCUUU CCUGGGAC
	1132	AGUCCCAG	CUGAUGA	Х	GAA	AAAGGGUU	AACCCUUUC CUGGGACU
	1154	UGCUCAAA	CUGAUGA	Х	GAA	ACAUCUUC	GAAGAUGUU UUUGAGCA
	1155	GUGCUCAA	CUGAUGA	X	GAA	AACAUCUU	AAGAUGUUU UUGAGCAC
	1156	GGUGCUCA	CUGAUGA	X	GAA	AAACAUCU	AGAUGUUUU UGAGCACC
30	1157	AGGUGCUC	CUGAUGA	Х	GAA	AAAACAUC	GAUGUUUUU GAGCACCU

	1166	CUAUUGUC	CUGAUGA	X	GAA	AGGUGCUC	GAGCACCUU	GACAAUAG
	1173	ACACUUUC	CUGAUGA	X	GAA	AUUGUCAA	UUGACAAUA	GAAAGUGU
	1205	CACAGGUG	CUGAUGA	X	GAA	AUUCCCCU	AGGGGAAUA	CACCUGUG
	1215	CUGGACGC	CUGAUGA	X	GAA	ACACAGGU	ACCUGUGUA	GCGUCCAG
5	1220	GUCCACUG	CUGAUGA	X	GAA	ACGCUACA	UGUAGCGUC	CAGUGGAC
	1236	υυυςυςυυ	CUGAUGA	X	GAA	AUCAUCCG	CGGAUGAUC	AAGAGAAA
	1246	AAAUGUUC	CUGAUGA	Х	GAA	AUUUCUCU	AGAGAAAUA	GAACAUUU
	1253	CUCGGACA	CUGAUGA	Х	GAA	AUGUUCUA	UAGAACAUU	UGUCCGAG
	1254	ACUCGGAC	CUGAUGA	X	GAA	AAUGUUCU	AGAACAUUU	GUCCGAGU
10	1257	UGAACUCG	CUGAUGA	X	GAA	ACAAAUGU	ACAUUUGUC	CGAGUUCA
	1263	UUUGUGUG	CUGAUGA	Х	GAA	ACUCGGAC	GUCCGAGUU	CACACAAA
	1264	CUUUGUGU	CUGAUGA	Х	GAA	AACUCGGA	UCCGAGUUC	ACACAAAG
	1276	AGCAAUAA	CUGAUGA	Х	GAA	AGGCUUUG	CAAAGCCUU	UUAUUGCU
	1277	AAGCAAUA	CUGAUGA	Х	GAA	AAGGCUUU	AAAGCCUUU	UAUUGCUU
15	1278	AAAGCAAU	CUGAUGA	Х	GAA	AAAGGCUU	AAGCCUUUU	AUUGCUUU
	1279	GAAAGCAA	CUGAUGA	X	GAA	AAAAGGCU	AGCCUUUUA	UUGCUUUC
	1281	CCGAAAGC	CUGAUGA	Х	GAA	AUAAAAGG	CCUUUUAUU	GCUUUCGG
	1285	ACUACCGA	CUGAUGA	Х	GAA	AGCAAUAA	UUAUUGCUU	UCGGUAGU
	1286	CACUACCG	CUGAUGA	X	GAA	AAGCAAUA	UAUUGCUUU	CGGUAGUG
20	1287	CCACUACC	CUGAUGA	X	GAA	AAAGCAAU	AUUGCUUUC	GGUAGUGG
	1291	CAUCCCAC	CUGAUGA	Х	GAA	ACCGAAAG	CUUUCGGUA	GUGGGAUG
	1304	CCACCAAA	CUGAUGA	X	GAA	AUUUCAUC	GAUGAAAUC	UUUGGUGG
	1306	UUCCACCA	CUGAUGA	Х	GAA	AGAUUUCA	UGAAAUCUU	UGGUGGAA
	1307	CUUCCACC	CUGAUGA	Х	GAA	AAGAUUUC	GAAAUCUUU	GGUGGAAG
2 5	1330	UCGGACUU	CUGAUGA	Х	GAA	ACUGCCCA	UGGGCAGUC	AAGUCCGA
	1335	GGGAUUCG	CUGAUGA	х	GAA	ACUUGACU	AGUCAAGUC	CGAAUCCC
	1341	UUCACAGG	CUGAUGA	Х	GAA	AUUCGGAC	GUCCGAAUC	CCUGUGAA
	1352	AACUGAGA	CUGAUGA	Х	GAA	ACUUCACA	UGUGAAGUA	UCUCAGUU
	1354	GUAACUGA	CUGAUGA	Х	GAA	AUACUUCA	UGAAGUAUC	UCAGUUAC
30	1356	GGGUAACU	CUGAUGA	X	GAA	AGAUACUU	AAGUAUCUC	AGUUACCC

	1360	AGCUGGGU	J CUGAUGA	X	GAA	A ACUGAGAU	AUCUCAGU	J ACCCAGCU
	1361	GAGCUGGC	CUGAUGA	X	GAA	AACUGAGA	UCUCAGUU	CCCAGCUC
	1369	GAUAUCAC	CUGAUGA	Х	GAA	AGCUGGGU	ACCCAGCU	CUGAUAUC
	1375	CCAUUUGA	CUGAUGA	X	GAA	AUCAGGAG	CUCCUGAU	UCAAAUGG
5	1377	UACCAUUU	CUGAUGA	. х	GAA	AUAUCAGG	CCUGAUAU	AAAUGGUA
	1385	CAUUUCUG	CUGAUGA	. X	GAA	ACCAUUUG	CAAAUGGUA	CAGAAAUG
	1404	UUGGACUC	CUGAUGA	. X	GAA	AUGGGCCU	AGGCCCAU	J GAGUCCAA
	1409	UGUAGUUG	CUGAUGA	X	GAA	ACUCAAUG	CAUUGAGUC	CAACUACA
	1415	UCAUUGUG	CUGAUGA	Х	GAA	AGUUGGAC	GUCCAACUA	CACAAUGA
10	1425	UCGCCAAC	CUGAUGA	X	GAA	AUCAUUGU	ACAAUGAUU	GUUGGCGA
	1428	UCAUCGCC	CUGAUGA	X	GAA	ACAAUCAU	AUGAUUGUU	GGCGAUGA
	1440	AUGAUGGU	CUGAUGA	Х	GAA	AGUUCAUC	GAUGAACUC	ACCAUCAU
	1446	ACUUCCAU	CUGAUGA	X	GAA	AUGGUGAG	CUCACCAUC	AUGG AAG U
	1478	UGACCGUG	CUGAUGA	X	GAA	AGUUUCCU	AGGAAACUA	CACGGUCA
15	1485	GUGAGGAU	CUGAUGA	X	GAA	ACCGUGUA	UACACGGUC	AUCCUCAC
•	1488	UUGGUGAG	CUGAUGA	X	GAA	AUGACCGU	ACGGUCAUC	CUCACCAA
	1491	GGGUUGGU	CUGAUGA	X	GAA	AGGAUGAC	GUCAUCCUC	ACCAACCC
	1503	UCCAUUGA	CUGAUGA	X	GAA	AUGGGGUU	AACCCCAUU	UCAAUGGA
	1504	CUCCAUUG	CUGAUGA	X	GAA	AAUGGGGU	ACCCCAUUU	CAAUGGAG
20	1505	UCUCCAUU	CUGAUGA	X	GAA	AAAUGGGG	CCCCAUUUC	AAUGGAGA
	1530	ACCAGAGA	CUGAUGA	Х	GAA	ACCAUGUG	CACAUGGUC	UCUCUGGU
	1532	CAACCAGA	CUGAUGA	X	GAA	AGACCAUG	CAUGGUCUC	UCUGGUUG
	1534	CACAACCA	CUGAUGA	X	GAA	AGAGACCA	UGGUCUCUC	UGGUUGUG
	1539	ACAUUCAC	CUGAUGA	Х	GAA	ACCAGAGA	UCUCUGGUU	GUGAAUGU
25	1548	UGGGGUGG	CUGAUGA	X	GAA	ACAUUCAC	GUGAAUGUC	CCACCCCA
	1560	UUCUCACC	CUGAUGA	X	GAA	AUCUGGGG	CCCCAGAUC	GGUGAGAA
							GAAAGCCUU	
							GCCUUGAUC	
							CUUGAUCUC	
30	1585	GGAAUCCA	CUGAUGA	X	GAA	AGGCGAGA	UCUCGCCUA	UGGAUUCC

	1591	CUGGUAGG	CUGAUGA	X	GAA	AUCCAUAG	CUAUGGAUU CCUACCAG
	1592	ACUGGUAG	CUGAUGA	X	GAA	AAUCCAUA	UAUGGAUUC CUACCAGU
	1595	CAUACUGG	CUGAUGA	X	GAA	AGGAAUCC	GGAUUCCUA CCAGUAUG
	1601	UGGUCCCA	CUGAUGA	X	GAA	ACUGGUAG	CUACCAGUA UGGGACCA
5	1619	UGCAUGUC	CUGAUGA	. X	GAA	AUGUCUGC	GCAGACAUU GACAUGCA
	1632	UUGGCGUA	CUGAUGA	X	GAA	ACUGUGCA	UGCACAGUC UACGCCAA
	1634	GGUUGGCG	CUGAUGA	X	GAA	AGACUGUG	CACAGUCUA CGCCAACC
	1645	GUGCAGGG	CUGAUGA	X	GAA	AGGGUUGG	CCAACCCUC CCCUGCAC
	1659	UACCACUG	CUGAUGA	Х	GAA	AUGUGGUG	CACCACAUC CAGUGGUA
10	1667	GCUGCCAG	CUGAUGA	Х	GAA	ACCACUGG	CCAGUGGUA CUGGCAGC
	1677	GCUUCUUC	CUGAUGA	X	GAA	AGCUGCCA	UGGCAGCUA GAAGAAGC
	1691	GUCUGUAG	CUGAUGA	х	GAA	AGCAGGCU	AGCCUGCUC CUACAGAC
	1694	CGGGUCUG	CUGAUGA	X	GAA	AGGAGCAG	CUGCUCCUA CAGACCCG
	1718	UACAAGCA	CUGAUGA	х	GAA	ACGGGCUU	AAGCCCGUA UGCUUGUA
15	1723	UUCUUUAC	CUGAUGA	Х	GAA	AGCAUACG	CGUAUGCUU GUAAAGAA
	1726	CCAUUCUU	CUGAUGA	X	GAA	ACAAGCAU	AUGCUUGUA AAGAAUGG
	1750	CCCCUGGA	CUGAUGA	X	GAA	AUCCUCCA	UGGAGGAUU UCCAGGGG
	1751	CCCCCUGG	CUGAUGA	Х	GAA	AAUCCUCC	GGAGGAUUU CCAGGGGG
	1752	CCCCCCUG	CUGAUGA	Х	GAA	AAAUCCUC	GAGGAUUUC CAGGGGGG
20	1770	GUGACUUC	CUGAUGA	Х	GAA	AUCUUGUU	AACAAGAUC GAAGUCAC
	1776	UUUUUGGU	CUGAUGA	Х	GAA	ACUUCGAU	AUCGAAGUC ACCAAAAA
	1790	UCAGGGCA	CUGAUGA	Х	GAA	AUUGGUUU	AAACCAAUA UGCCCUGA
	1800	UUUCCUUC	CUGAUGA	Х	GAA	AUCAGGGC	GCCCUGAUU GAAGGAAA
	1821	AGCGUACU	CUGAUGA	Х	GAA	ACAGUUUU	AAAACUGUA AGUACGCU
25		GACCAGCG					CUGUAAGUA CGCUGGUC
	1833	GCUUGGAU	CUGAUGA	X	GAA	ACCAGCGU	ACGCUGGUC AUCCAAGC
	1836	GCAGCUUG	CUGAUGA	Х	GAA	AUGACCAG	CUGGUCAUC CAAGCUGC
	1853	ACAACGCU	CUGAUGA	Х	GAA	ACACGUUG	CAACGUGUC AGCGUUGU
	1859	AUUUGUAC	CUGAUGA	X	GAA	ACGCUGAC	GUCAGCGUU GUACAAAU
30	1862	CACAUUUG	CUGAUGA	X	GAA	ACAACGCU	AGCGUUGUA CAAAUGUG

	1878	GCUUUGU	J CUGAUG	A X	(GA	A AUGGCUUC	GAAGCCAUC AACAAAGC
						A ACCCUCUC	Combo .E.C.EEAOC
						AUGACCCU	The state of the s
						AGAUGACC	AGGGUCAUC UCCUUCCA
5						AGGAGAUG	GGUCAUCUC CUUCCAUG
J						AAGGAGAU	CAUCUCCUU CCAUGUGA
						AUCACAUG	AUCUCCUUC CAUGUGAU
							CAUGUGAUC AGGGGUCC
						ACCCCUGA	
• •						AUUUCAGG	CCUGAAAUU ACUGUGCA
10						AAUUUCAG	CUGAAAUUA CUGUGCAA
						ACACACUC	GAGUGUGUC CCUGUUGU
	1988	CAGUGCAC	CUGAUGA	X	GAA	ACAGGGAC	GUCCCUGUU GUGCACUG
	2008	CUCAAACG	CUGAUGA	X	GAA	AUUUCUGU	ACAGAAAUA CGUUUGAG
	2012	GGUUCUCA	CUGAUGA	Х	GAA	ACGUAUUU	AAAUACGUU UGAGAACC
1 5	2013	AGGUUCUC	CUGAUGA	X	GAA	AACGUAUU	AAUACGUUU GAGAACCU
	2022	UACCACGU	CUGAUGA	Х	GAA	AGGUUCUC	GAGAACCUC ACGUGGUA
	2030	CAAGCUUG	CUGAUGA	X	GAA	ACCACGUG	CACGUGGUA CAAGCUUG
	2037	UGUGAGCC	CUGAUGA	Х	GAA	AGCUUGUA	UACAAGCUU GGCUCACA
	2042	UUGCCUGU	CUGAUGA	Х	GAA	AGCCAAGC	GCUUGGCUC ACAGGCAA
20	2054	UGUGGACC	CUGAUGA	х	GAA	AUGUUGCC	GGCAACAUC GGUCCACA
	2058	CCCAUGUG	CUGAUGA	х	GAA	ACCGAUGU	ACAUCGGUC CACAUGGG
	2072	GUGUGAGU	CUGAUGA	х	GAA	AUUCGCCC	GGGCGAAUC ACUCACAC
	2076	ACUGGUGU	CUGAUGA	х	GAA	AGUGAUUC	GAAUCACUC ACACCAGU
	2085	UUCUUGCA	CUGAUGA	х	GAA	ACUGGUGU	ACACCAGUU UGCAAGAA
25	2086	GUUCUUGC	CUGAUGA	х	GAA	AACUGGUG	CACCAGUUU GCAAGAAC
	2096	GAGCAUCC	CUGAUGA	х	GAA	AGUUCUUG	CAAGAACUU GGAUGCUC
	2104	UUUCCAAA	CUGAUGA	х	GAA	AGCAUCCA	UGGAUGCUC UUUGGAAA
	2106	AGUUUCCA	CUGAUGA	х	GAA	AGAGCAUC	GAUGCUCUU UGGAAACU
	2107	CAGUUUCC	CUGAUGA	Х	GAA	AAGAGCAU	AUGCUCUUU GGAAACUG
30						ACAUGGUG	CACCAUGUU UUCUAACA
							ELISCITOCOC OCCUANCA

	2130	CUGUUAGA	CUGAUGA	X	GAA	AACAUGGU	ACCAUGUUU	UCUAACAG
	2131	GCUGUUAG	CUGAUGA	х	GAA	AAACAUGG	CCAUGUUUU	CUAACAGC
	2132	UGCUGUUA	CUGAUGA	Х	GAA	AAAACAUG	CAUGUUUUC	UAACAGCA
	2134	UGUGCUGU	CUGAUGA	Х	GAA	AGAAAACA	UGUUUUCUA	ACAGCACA
5	2151	ACAAUCAA	CUGAUGA	х	GAA	AUGUCAUU	AAUGACAUC	UUGAUUGU
	2153	CCACAAUC	CUGAUGA	х	GAA	AGAUGUCA	UGACAUCUU	GAUUGUGG
	2157	AAUGCCAC	CUGAUGA	x	GAA	AUCAAGAU	AUCUUGAUU	GUGGCAUU
	2165	CAUUCUGA	CUGAUGA	х	GAA	AUGCCACA	UGUGGCAUU	UCAGAAUG
	2166	GCAUUCUG	CUGAUGA	х	GAA	AAUGCCAC	GUGGCAUUU	CAGAAUGC
10	2167	GGCAUUCU	CUGAUGA	Х	GAA	AAAUGCCA	UGGCAUUUC	AGAAUGCC
	2177	CCUGCAGA	CUGAUGA	х	GAA	AGGCAUUC	GAAUGCCUC	UCUGCAGG
	2179	GUCCUGCA	CUGAUGA	X	GAA	AGAGGCAU	AUGCCUCUC	UGCAGGAC
	2198	AGCAAACA	CUGAUGA	x	GAA	AGUCGCCU	AGGCGACUA	UGUUUGCU
	2202	GCAGAGCA	CUGAUGA	x	GAA	ACAUAGUC	GACUAUGUU	UGCUCUGC
15	2203	AGCAGAGC	CUGAUGA	x	GAA	AACAUAGU	ACUAUGUUU	GCUCUGCU
	2207	CUUGAGCA	CUGAUGA	X	GAA	AGCAAACA	UGUUUGCUC	UGCUCAAG
	2212	CUUAUCUU	CUGAUGA	Х	GAA	AGCAGAGC	GCUCUGCUC	AAGAUAAG
	2218	GGUCUUCU	CUGAUGA	x	GAA	AUCUUGAG	CUCAAGAUA	AGAAGACC
	2239	GACCAGGC	CUGAUGA	Х	GAA	AUGUCUUU	AAAGACAUU	GCCUGGUC
20	2247	AGCUGUUU	CUGAUGA	x	GAA	ACCAGGCA	UGCCUGGUC	AAACAGCU
	2256	AGGAUGAU	CUGAUGA	X	GAA	AGCUGUUU	AAACAGCUC	AUCAUCCU
	2259	UCUAGGAU	CUGAUGA	х	GAA	AUGAGCUG	CAGCUCAUC	AUCCUAGA
	2262	CGCUCUAG	CUGAUGA	X	GAA	AUGAUGAG	CUCAUCAUC	CUAGAGCG
	2265	AUGCGCUC	CUGAUGA	х	GAA	AGGAUGAU	AUCAUCCUA	GAGCGCAU
25	2286	UUUCCGGU	CUGAUGA	х	GAA	AUCAUGGG	CCCAUGAUC	ACCGGAAA
	2296	AUUCUCCA	CUGAUGA	х	GAA	AUUUCCGG	CCGGAAAUC	UGGAGAAU
	2305	UGUUGUCU	CUGAUGA	х	GAA	AUUCUCCA	UGGAGAAUC	AGACAACA
	2319	GUCUCGCC	CUGAUGA	х	GAA	AUGGUU GU	ACAACCAUU	GGCGAGAC
	2331	GUCACUUC	CUGAUGA	Х	GAA,	AUGGUCUC	GAGACCAUU	GAAGUGAC
30	2341	UGCUGGGC	CUGAUGA	X	GAA	AGUCACUU	AAGUGACUU	GCCCAGCA

	2351 GAUUUCCA CUGAUGA X GAA AUGCUGGG	CCCAGCAUC UGGAAAUC
	2359 UGGGGUAG CUGAUGA X GAA AUUUCCAG	CUGGAAAUC CUACCCCA
	2362 GUGUGGGG CUGAUGA X GAA AGGAUUUC	GAAAUCCUA CCCCACAC
	2373 AACCAUGU CUGAUGA X GAA AUGUGUGG	CCACACAUU ACAUGGUU
5	2374 GAACCAUG CUGAUGA X GAA AAUGUGUG	CACACAUUA CAUGGUUC
	2381 UGUCUUUG CUGAUGA X GAA ACCAUGUA	UACAUGGUU CAAAGACA
	2382 UUGUCUUU CUGAUGA X GAA AACCAUGU	ACAUGGUUC AAAGACAA
	2403 GAAUCUUC CUGAUGA X GAA ACCAGGGU	ACCCUGGUA GAAGAUUC
	2410 AAUGCCUG CUGAUGA X GAA AUCUUCUA	UAGAAGAUU CAGGCAUU
10	2411 CAAUGCCU CUGAUGA X GAA AAUCUUCU	AGAAGAUUC AGGCAUUG
	2418 CUCAGUAC CUGAUGA X GAA AUGCCUGA	UCAGGCAUU GUACUGAG
	2421 UCUCUCAG CUGAUGA X GAA ACAAUGCC	GGCAUUGUA CUGAGAGA
	2449 CCUGCGGA CUGAUGA X GAA AGUCAGGU	ACCUGACUA UCCGCAGG
	2451 ACCCUGCG CUGAUGA X GAA AUAGUCAG	CUGACUAUC CGCAGGGU
15	2481 CAGGUGUA CUGAUGA X GAA AGGCCUCC	GGAGGCCUC UACACCUG
	2483 GGCAGGUG CUGAUGA X GAA AGAGGCCU	AGGCCUCUA CACCUGCC
	2505 CAGCCAAG CUGAUGA X GAA ACAUUGCA	UGCAAUGUC CUUGGCUG
	2508 GCACAGCC CUGAUGA X GAA AGGACAUU	AAUGUCCUU GGCUGUGC
	2532 AUUAUGAA CUGAUGA X GAA AGCGUCUC	GAGACGCUC UUCAUAAU
20	2534 CUAUUAUG CUGAUGA X GAA AGAGCGUC	GACGCUCUU CAUAAUAG
	2535 UCUAUUAU CUGAUGA X GAA AAGAGCGU	ACGCUCUUC AUAAUAGA
	2538 CCUUCUAU CUGAUGA X GAA AUGAAGAG	CUCUUCAUA AUAGAAGG
	2541 GCACCUUC CUGAUGA X GAA AUUAUGAA	UUCAUAAUA GAAGGUGC
	2567 UGACUUCC CUGAUGA X GAA AGUUGGUC	GACCAACUU GGAAGUCA
25	2574 AGGAUAAU CUGAUGA X GAA ACUUCCAA	UUGGAAGUC AUUAUCCU
	2577 ACGAGGAU CUGAUGA X GAA AUGACUUC	GAAGUCAUU AUCCUCGU
	2578 GACGAGGA CUGAUGA X GAA AAUGACUU	AAGUCAUUA UCCUCGUC
	2580 CCGACGAG CUGAUGA X GAA AUAAUGAC	GUCAUUAUC CUCGUCGG
	2583 GUGCCGAC CUGAUGA X GAA AGGAUAAU	AUUAUCCUC GUCGGCAC
30	2586 GCAGUGCC CUGAUGA X GAA ACGAGGAU	AUCCUCGUC GGCACUGC

WO 97/15662

134

PCT/US96/17480

	2601	AACAUGGC	CUGAUGA	X	GAA	AUCACUGC	GCAGUGAUU	GCCAUGUU
	2609	GCCAGAAG	CUGAUGA	X	GAA	ACAUGGCA	UGCCAUGUU	CUUCUGGC
	2610	AGCCAGAA	CUGAUGA	X	GAA	AACAUGGC	GCCAUGUUC	UUCUGGCU
	2612	GGAGCCAG	CUGAUGA	X	GAA	AGAACAUG	CAUGUUCUU	CUGGCUCC
5	2613	AGGAGCCA	CUGAUGA	х	GAA	AAGAACAU	AUGUUCUUC	UGGCUCCU
	2619	ACAAGAAG	CUGAUGA	X	GAA	AGCCAGAA	UUCUGGCUC	CUUCUUGU
	2622	AUGACAAG	CUGAUGA	Х	GAA	AGGAGCCA	UGGCUCCUU	CUUGUCAU
	2623	AAUGACAA	CUGAUGA	X	GAA	AAGGAGCC	GGCUCCUUC	UUGUCAUU
	2625	ACAAUGAC	CUGAUGA	X	GAA	AGAAGGAG	cuccuucuu	GUCAUUGU
10	2628	AGGACAAU	CUGAUGA	X	GAA	ACAAGAAG	CUUCUUGUC	AUUGUCCU
	2631	CGUAGGAC	CUGAUGA	Х	GAA	AUGACAAG	CUUGUCAUU	GUCCUACG
	2634	GUCCGUAG	CUGAUGA	Х	GAA	ACAAUGAC	GUCAUUGUC	CUACGGAC
	2637	ACGGUCCG	CUGAUGA	X	GAA	AGGACAAU	AUUGUCCUA	CGGACCGU
	2646	GCCCGCUU	CUGAUGA	X	GAA	ACGGUCCG	CGGACCGUU	AAGCGGGC
15	2647	GGCCCGCU	CUGAUGA	X	GAA	AACGGUCC	GGACCGUUA	AGCGGGCC
	2681	UAGACAAG	CUGAUGA	X	GAA	AGCCUGUC	GACAGGCUA	CUUGUCUA
	2684	CAAUAGAC	CUGAUGA	X	GAA	AGUAGCCU	AGGCUACUU	GUCUAUUG
	2687	UGACAAUA	CUGAUGA	X	GAA	ACAAGUAG	CUACUUGUC	UAUUGUCA
	2689	CAUGACAA	CUGAUGA	X	GAA	AGACAAGU	ACUUGUCUA	UUGUCAUG
20	2691	UCCAUGAC	CUGAUGA	X	GAA	AUAGACAA	UUGUCUAUU	GUCAUGGA
	2694	GGAUCCAU	CUGAUGA	X	GAA	ACAAUAGA	UCUAUUGUC	AUGGAUCC
	2701	UUCAUCUG	CUGAUGA	Х	GAA	AUCCAUGA	UCAUGGAUC	CAGAUGAA
	2711	CCAAGGGC	CUGAUGA	X	GAA	AUUCAUCU	AGAUGAAUU	GCCCUUGG
	2717	GCUCAUCC	CUGAUGA	Х	GAA	AGGGCAAU	AUUGCCCUU	GGAUGAGC
25	2738	CAUAAGGC	CUGAUGA	Х	GAA	AGCGUUCA	UGAACGCUU	GCCUUAUG
	2743	GGCAUCAU	CUGAUGA	Х	GAA	AGGCAAGC	GCUUGCCUU	AUGAUGCC
	2744	UGGCAUCA	CUGAUGA	Х	GAA	AAGGCAAG	CUUGCCUUA	UGAUGCCA
	2765	CCCUGGGG	CUGAUGA	X	GAA	AUUCCCAC	GUGGGAAUU	CCCCAGGG
	2766	UCCCUGGG	CUGAUGA	Х	GAA	AAUUCCCA	UGGGAAUUC	CCCAGGGA
30	2787	GGUUUUCC	CUGAUGA	Χ	GAA	AGUUUCAG	CUGAAACUA	GGAAAACC

WO 97/15662

	279	7 GCGGCCA	A CUGAUGA	λ >	(GAA	AGGUUUUC	GAAAACCUC UUGGCCGC
	279	9 CCGCGGC	CUGAUGA	X	GAA	AGAGGUUU	AAACCUCUU GGCCGCGG
	281	3 CUUGGCCC	G CUGAUGA	X	GAA	AGGCACCG	CGGUGCCUU CGGCCAAG
	2814	ACUUGGC	CUGAUGA	X	GAA	AAGGCACC	GGUGCCUUC GGCCAAGU
5	2826	UCUGCCUC	CUGAUGA	Х	GAA	AUCACUUG	CAAGUGAUU GAGGCAGA
	2839	AAUUCCAA	CUGAUGA	. х	GAA	AGCGUCUG	CAGACGCUU UUGGAAUU
	2840	CAAUUCCA	CUGAUGA	X	GAA	AAGCGUCU	AGACGCUUU UGGAAUUG
	2841	. UCAAUUCC	CUGAUGA	. X	GAA	AAAGCGUC	GACGCUUUU GGAAUUGA
	2847	gucuuguc	CUGAUGA	X	GAA	AUUCCAAA	UUUGGAAUU GACAAGAC
10	2863	UGUUUUGC	CUGAUGA	Х	GAA	AGUCGCUG	CAGCGACUU GCAAAACA
	2874	UUGACGGC	CUGAUGA	X	GAA	ACUGUUUU	AAAACAGUA GCCGUCAA
	2880	AACAUCUU	CUGAUGA	X	GAA	ACGGCUAC	GUAGCCGUC AAGAUGUU
	2888	CUUCUUUC	CUGAUGA	Х	GAA	ACAUCUUG	CAAGAUGUU GAAAGAAG
	2917	GAGGGCUC	CUGAUGA	X	GAA	AUGCUCGC	GCGAGCAUC GAGCCCUC
15	2925	UCAGACAU	CUGAUGA	Х	GAA	AGGGCUCG	CGAGCCCUC AUGUCUGA
	2930	UGAGUUCA	CUGAUGA	X	GAA	ACAUGAGG	CCUCAUGUC UGAACUCA
	2937	AGGAUCUU	CUGAUGA	Х	GAA	AGUUCAGA	UCUGAACUC AAGAUCCU
	2943	UGGAUGAG	CUGAUGA	X	GAA	AUCUUGAG	CUCAAGAUC CUCAUCCA
	2946	AUGUGGAU	CUGAUGA	Х	GAA	AGGAUCUU	AAGAUCCUC AUCCACAU
20	2949	CCAAUGUG	CUGAUGA	Х	GAA	AUGAGGAU	AUCCUCAUC CACAUUGG
	2955	UGGUGACC	CUGAUGA	X	GAA	AUGUGGAU	AUCCACAUU GGUCACCA
	2959	GAGAUGGU	CUGAUGA	Х	GAA	ACCAAUGU	ACAUUGGUC ACCAUCUC
	2965	CACAUUGA	CUGAUGA	X	GAA	AUGGUGAC	GUCACCAUC UCAAUGUG
	2967	ACCACAUU	CUGAUGA	Х	GAA	AGAUGGUG	CACCAUCUC AAUGUGGU
2 5	2982	GCGCCUAG	CUGAUGA	Х	GAA	AGGUUCAC	GUGAACCUC CUAGGCGC
	2985	CAGGCGCC	CUGAUGA	X	GAA	AGGAGGUU	AACCUCCUA GGCGCCUG
	3013	CACCAUGA	CUGAUGA	X	GAA	AGGCCCUC	GAGGGCCUC UCAUGGUG
	3015	AUCACCAU	CUGAUGA	X	GAA .	AGAGGCCC	GGGCCUCUC AUGGUGAU
	3024	AAUUCCAC	CUGAUGA	X	GAA .	AUCACCAU	AUGGUGAUU GUGGAAUU
30	3032	ACUUGCAG	CUGAUGA	X	GAA .	AUUCCACA	UGUGGAAUU CUGCAAGU

	3033	AACUUGCA	CUGAUGA	Х	GAA	AAUUCCAC	GUGGAAUUC	UGCAAGUU
	3041	GGUUUCCA	CUGAUGA	Х	GAA	ACUUGCAG	CUGCAAGUU	UGGAAACC
	3042	AGGUUUCC	CUGAUGA	Х	GAA	AACUUGCA	UGCAAGUUU	GGAAACCU
	3051	UAAGUUGA	CUGAUGA	Х	GAA	AGGUUUCC	GGAAACCUA	UCAACUUA
5	3053	AGUAAGUU	CUGAUGA	Х	GAA	AUAGGUUU	AAACCUAUC	AACUUACU
	3058	CCGUAAGU	CUGAUGA	X	GAA	AGUUGAUA	UAUCAACUU	ACUUACGG
	3059	CCCGUAAG	CUGAUGA	X	GAA	AAGUUGAU	AUCAACUUA	CUUACGGG
	3062	UGCCCCGU	CUGAUGA	Х	GAA	AGUAAGUU	AACUUACUU	ACGGGGCA
	3063	UUGCCCCG	CUGAUGA	Х	GAA	AAGUAAGU	ACUUACUUA	CGGGGCAA
10	3083	AGGGAACA	CUGAUGA	X	GAA	AUUCAUUU	AAAUGAAUU	UGUUCCCU
	3084	UAGGGAAC	CUGAUGA	Х	GAA	AAUUCAUU	AAUGAAUUU	GUUCCCUA
	3087	UUAUAGGG	CUGAUGA	Х	GAA	ACAAAUUC	GAAUUUGUU	CCCUAUAA
	3088	CUUAUAGG	CUGAUGA	Х	GAA	AACAAAUU	AAUUUGUUC	CCUAUAAG
	3092	UGCUCUUA	CUGAUGA	Х	GAA	AGGGAACA	UGUUCCCUA	UAAGAGCA
15	3094	UUUGCUCU	CUGAUGA	Х	GAA	AUAGGGAA	UUCCCUAUA	AGAGCAAA
	3113	CCUGGCGG	CUGAUGA	Х	GAA	AGCGUGCC	GGCACGCUU	CCGCCAGG
	3114	CCCUGGCG	CUGAUGA	X	GAA	AAGCGUGC	GCACGCUUC	CGCCAGGG
	3131	CCCCAACG	CUGAUGA	х	GAA	AGUCCUUG	CAAGGACUA	CGUUGGGG
	31 35	AGCUCCCC	CUGAUGA	Х	GAA	ACGUAGUC	GACUACGUU	GGGGAGCU
20	3144	UCCACGGA	CUGAUGA	Х	GAA	AGCUCCCC	GGGGAGCUC	UCCGUGGA
	3146	GAUCCACG	CUGAUGA	х	GAA	AGAGCUCC	GGAGCUCUC	CGUGGAUC
	3154	UCUUUUCA	CUGAUGA	х	GAA	AUCCACGG	CCGUGGAUC	UGAAAAGA
	3167	UGCUGUCC	CUGAUGA	Х	GAA	AGCGUCUU	AAGACGCUU	GGACAGCA
	3177	CUGCUGGU	CUGAUGA	Х	GAA	AUGCUGUC	GACAGCAUC	ACCAGCAG
25	3194	AGCUGGCA	CUGAUGA	Х	GAA	AGCUCUGG	CCAGAGCUC	UGCCAGCU
	3203	CAAAGCCU	CUGAUGA	Х	GAA	AGCUGGCA	UGCCAGCUC	AGGCUUUG
	3209	CCUCAACA	CUGAUGA	Х	GAA	AGCCUGAG	CUCAGGCUU	UGUUGAGG
	3210	UCCUCAAC	CUGAUGA	Х	GAA	AAGCCUGA	UCAGGCUUU	GUUGAGGA
	3213	UUCUCCUC	CUGAUGA	Х	GAA	ACAAAGCC	GGCUUUGUU	GAGGAGAA
30	3224	CACUGAGC	CUGAUGA	Х	GAA	AUUUCUCC	GGAGAAAUC	GCUCAGUG

	3228	ACAUCACU	CUGAUGA	X	GA,A	AGCGAUUU	AAAUCGCUC	AGUGAUGU
	3237	ucuuccuc	CUGAUGA	X	GAA	ACAUCACU	AGUGAUGUA	GAGGAAGA
	3253	UUCUUCAG	CUGAUGA	X	GAA	AGCUUCUU	AAGAAGCUU	CUGAAGAA
	3254	GUUCUUCA	CUGAUGA	Х	GAA	AAGCUUCU	AGAAGCUUC	UGAAGAAC
5	3266	AGUCCUUG	CUGAUGA	Х	GAA	ACAGUUCU	AGAACUGUA	CAAGGACU
	3275	AGGUCAGG	CUGAUGA	Х	GAA	AGUCCUUG	CAAGGACUU	CCUGACCU
	3276	AAGGUCAG	CUGAUGA	X	GAA	AAGUCCUU	AAGGACUUC	CUGACCUU
	3284	GAUGCUCC	CUGAUGA	X	GAA	AGGUCAGG	CCUGACCUU	GGAGCAUC
	3292	ACAGAUGA	CUGAUGA	X	GAA	AUGCUCCA	UGGAGCAUC	UCAUCUGU
10	3294	UAACAGAU	CUGAUGA	X	GAA	AGAUGCUC	GAGCAUCUC	AUCUGUUA
	3297	CUGUAACA	CUGAUGA	Х	GAA	AUGAGAUG	CAUCUCAUC	UGUUACAG
	3301	GAAGCUGU	CUGAUGA	X	GAA	ACAGAUGA	UCAUCUGUU	ACAGCUUC
	3302	GGAAGCUG	CUGAUGA	X	GAA	AACAGAUG	CAUCUGUUA	CAGCUUCC.
	3308	CCACUUGG	CUGAUGA	X	GAA	AGCUGUAA	UUACAGCUU	CCAAGUGG
15	3309	GCCACUUG	CUGAUGA	X	GAA	AAGCUGUA	UACAGCUUC	CAAGUGGC
	3319	CAUGCCCU	CUGAUGA	X	GAA	AGCCACUU	AAGUGGCUA	AGGGCAUG
	3332	AUGCCAAG	CUGAUGA	Х	GAA	ACUCCAUG	CAUGGAGUU	CUUGGCAU
	3333	GAUGCCAA	CUGAUGA	X	GAA	AACUCCAU	AUGGAGUUC	UUGGCAUC
	3335	UUGAUGCC	CUGAUGA	X	GAA	AGAACUCC	GGAGUUCUU	GGCAUCAA
20	3341	ACUUCCUU	CUGAUGA	X	GAA	AUGCCAAG	CUUGGCAUC	AAGGAAGU
	3352	CCUGUGGA	CUGAUGA	X	GAA	ACACUUCC	GGAAGUGUA	UCCACAGG
	3354	UCCCUGUG	CUGAUGA	X	GAA	AUACACUU	AAGUGUAUC	CACAGGGA
	3381	GAUAGGAG	CUGAUGA	X	GAA	AUGUUUCG	CGAAACAUU	CUCCUAUC
	3382	CGAUAGGA	CUGAUGA	X	GAA	AAUGUUUC	GAAACAUUC	UCCUAUCG
25	3384	UCCGAUAG	CUGAUGA	X	GAA	AGAAUGUU	AACAUUCUC	CUAUCGGA
	3387	UUCUCCGA (CUGAUGA	X	GAA	AGGAGAAU	AUUCUCCUA	UCGGAGAA
	3389	טכטטכטככ (CUGAUGA	X	GAA	AUAGGAGA	UCUCCUAUC (GGAGAAGA
	3405	CAGAUCUU (CUGAUGA	X	GAA	ACCACAUU	AAUGUGGUU 2	AAGAUCUG
	3406	ACAGAUCU (CUGAUGA	X	GAA	AACCACAU	AUGUGGUUA 2	AGAUCUGU
30	3411	AAGUCACA (CUGAUGA :	X	GAA	AUCUUAAC	GUUAAGAUC 1	JGUGACUU

	3419	CCAAGCCG	CUGAUGA	X	GAA	AGUCACAG	CUGUGACUU CGGCUUGG
	3420	GCCAAGCC	CUGAUGA	X	GAA	AAGUCACA	UGUGACUUC GGCUUGGC
	3425	CCCGGGCC	CUGAUGA	X	GAA	AGCCGAAG	CUUCGGCUU GGCCCGGG
	3438	UCUUUAUA	CUGAUGA	. X	GAA	AUGUCCCG	CGGGACAUU UAUAAAGA
5	3439	GUCUUUAU	CUGAUGA	X	GAA	AAUGUCCC	GGGACAUUU AUAAAGAC
	3440	GGUCUUUA	CUGAUGA	Х	GAA	AAAUGUCC	GGACAUUUA UAAAGACC
	3442	CGGGUCUU	CUGAUGA	X	GAA	AUAAAUGU	ACAUUUAUA AAGACCCG
	3454	UCUGACAU	CUGAUGA	Х	GAA	AUCCGGGU	ACCCGGAUU AUGUCAGA
	3455	UUCUGACA	CUGAUGA	Х	GAA	AAUCCGGG	CCCGGAUUA UGUCAGAA
10	3459	CCUUUUCU	CUGAUGA	Х	GAA	ACAUAAUC	GAUUAUGUC AGAAAAGG
	3480	UUCAAAGG	CUGAUGA	X	GAA	AGUCGGGC	GCCCGACUC CCUUUGAA
	3484	CCACUUCA	CUGAUGA	X	GAA	AGGGAGUC	GACUCCCUU UGAAGUGG
	3485	UCCACUUC	CUGAUGA	X	GAA	AAGGGAGU	ACUCCCUUU GAAGUGGA
	3510	CUGUCAAA	CUGAUGA	X	GAA	AUGGUUUC	GAAACCAUU UUUGACAG
15	3511	UCUGUCAA	CUGAUGA	X	GAA	AAUGGUUU	AAACCAUUU UUGACAGA
	3512	CUCUGUCA	CUGAUGA	X	GAA	AAAUGGUU	AACCAUUUU UGACAGAG
	3513	ACUCUGUC	CUGAUGA	X	GAA	AAAAUGGU	ACCAUUUUU GACAGAGU
	3522	AUUGUGUA	CUGAUGA	X	GAA	ACUCUĞUC	GACAGAGUA UACACAAU
	3524	GAAUUGUG	CUGAUGA	Х	GAA	AUACUCUG	CAGAGUAUA CACAAUUC
20	3531	UCGCUCUG	CUGAUGA	X	GAA	AUUGUGUA	UACACAAUU CAGAGCGA
	3532	AUCGCUCU	CUGAUGA	Х	GAA	AAUUGUGU	ACACAAUUC AGAGCGAU
	3548	CACCGAAA	CUGAUGA	Х	GAA	ACCACACA	UGUGUGGUC UUUCGGUG
	3550	CACACCGA	CUGAUGA	Х	GAA	AGACCACA	UGUGGUCUU UCGGUGUG
	3551	ACACACCG	CUGAUGA	Х	GAA	AAGACCAC	GUGGUCUUU CGGUGUGU
25	3552	AACACACC	CUGAUGA	X	GAA	AAAGACCA	UGGUCUUUC GGUGUGUU
	3560	CCCAGAGC	CUGAUGA	X	GAA	ACACACCG	CGGUGUGUU GCUCUGGG
	3564	AUUUCCCA	CUGAUGA	Х	GAA	AGCAACAC	GUGUUGCUC UGGGAAAU
	3573	AAGGAAAA	CUGAUGA	X	GAA	AUUUCCCA	UGGGAAAUA UUUUCCUU
		CUAAGGAA					GGAAAUAUU UUCCUUAG
30	3576	CCUAAGGA	CUGAUGA	X	GAA	AAUAUUUC	GAAAUAUUU UCCUUAGG

÷,

	3577 ACCUAAGG CUGAUGA X GAA AAAUAUUU	AAAUAUUUU CCUUAGGU
	3578 CACCUAAG CUGAUGA X GAA AAAAUAUU	AAUAUUUUC CUUAGGUG
	3581 AGGCACCU CUGAUGA X GAA AGGAAAAU	AUUUUCCUU AGGUGCCU
	3582 GAGGCACC CUGAUGA X GAA AAGGAAAA	UUUUCCUUA GGUGCCUC
5	3590 GGUAUGGG CUGAUGA X GAA AGGCACCU	AGGUGCCUC CCCAUACC
	3596 CCCCAGGG CUGAUGA X GAA AUGGGGAG	CUCCCCAUA CCCUGGGG
	3606 UCAAUCUU CUGAUGA X GAA ACCCCAGG	CCUGGGGUC AAGAUUGA
	3612 UCUUCAUC CUGAUGA X GAA AUCUUGAC	GUCAAGAUU GAUGAAGA
	3623 UCCUACAA CUGAUGA X GAA AUUCUUCA	UGAAGAAUU UUGUAGGA
10	3624 CUCCUACA CUGAUGA X GAA AAUUCUUC	GAAGAAUUU UGUAGGAG
	3625 UCUCCUAC CUGAUGA X GAA AAAUUCUU	AAGAAUUUU GUAGGAGA
	3628 CAAUCUCC CUGAUGA X GAA ACAAAAUU	AAUUUUGUA GGAGAUUG
	3635 CUUCUUUC CUGAUGA X GAA AUCUCCUA	UAGGAGAUU GAAAGAAG
	3649 CCGCAUUC CUGAUGA X GAA AGUUCCUU	AAGGAACUA GAAUGCGG
15	3661 GUAGUCAG CUGAUGA X GAA AGCCCGCA	UGCGGGCUC CUGACUAC
	3668 GGGUAGUG CUGAUGA X GAA AGUCAGGA	UCCUGACUA CACUACCĊ
	3673 UUCUGGGG CUGAUGA X GAA AGUGUAGU	ACUACACUA CCCCAGAA
	3686 UGGUCUGG CUGAUGA X GAA ACAUUUCU	AGAAAUGUA CCAGACCA
	3734 CUGAAAAC CUGAUGA X GAA AGGGUCUC	GAGACCCUC GUUUUCAG
20	3737 ACUCUGAA CUGAUGA X GAA ACGAGGGU	ACCCUCGUU UUCAGAGU
	3738 AACUCUGA CUGAUGA X GAA AACGAGGG	CCCUCGUUU UCAGAGUU
	3739 CAACUCUG CUGAUGA X GAA AAACGAGG	CCUCGUUUU CAGAGUUG
	3740 CCAACUCU CUGAUGA X GAA AAAACGAG	CUCGUUUUC AGAGUUGG
	3746 GCUCCACC CUGAUGA X GAA ACUCUGAA	UUCAGAGUU GGUGGAGC
25	3757 GUUUCCCA CUGAUGA X GAA AUGCUCCA	UGGAGCAUU UGGGAAAC
	3758 GGUUUCCC CUGAUGA X GAA AAUGCUCC	GGAGCAUUU GGGAAACC
	3768 GCUUGCAG CUGAUGA X GAA AGGUUUCC	GGAAACCUC CUGCAAGC
	3803 GAACAAUA CUGAUGA X GAA AGUCUUUG	CAAAGACUA UAUUGUUC
	3805 AAGAACAA CUGAUGA X GAA AUAGUCUU	AAGACUAUA UUGUUCUU
30	3807 GGAAGAAC CUGAUGA X GAA AUAUAGUC	GACUAUAUU GUUCUUCC

	3810	AUUGGAAG	CUGAUGA	X	GAA	ACAAUAUA	UAUAUUGUU	CUUCCAAU
	3811	CAUUGGAA	CUGAUGA	X	GAA	AACAAUAU	AUAUUGUUC	UUCCAAUG
	3813	GACAUUGG	CUGAUGA	X	GAA	AGAAC AA U	AUUGUUCUU	CCAAUGUC
	3814	UGACAUUG	CUGAUGA	Х	GAA	AAGAACAA	UUGUUCUUC	CAAUGUCA
5	3821	GUGUCUCU	CUGAUGA	X	GAA	ACAUUGGA	UCCAAUGUC	AGAGACAC
	3847	GAGUCCAG	CUGAUGA	Х	GAA	AUCCUCUU	AAGAGGAUU	CUGGACUC
	3848	AGAGUCCA	CUGAUGA	Х	GAA	AAUCCUCU	AGAGGAUUC	UGGACUCU
	3855	GGCAGGGA	CUGAUGA	Х	GAA	AGUCCAGA	UCUGGACUC	UCCCUGCC
	3857	UAGGCAGG	CUGAUGA	Х	GAA	AGAGUCCA	UGGACUCUC	CCUGCCUA
10	3865	AGGUGAGG	CUGAUGA	Х	GAA	AGGCAGGG	CCCUGCCUA	CCUCACCU
	3869	AAACAGGU	CUGAUGA	Х	GAA	AGGUAGGC	GCCUACCUC	ACCUGUUU
	3876	AUACAGGA	CUGAUGA	Х	GAA	ACAGGUGA	UCACCUGUU	UCCUGUAU
	3877	CAUACAGG	CUGAUGA	х	GAA	AACAGGUG	CACCUGUUU	CCUGUAUG
	3878	CCAUACAG	CUGAUGA	Х	GAA	AAACAGGU	ACCUGUUUC	CUGUAUGG
15	3883	UUCCUCCA	CUGAUGA	Х	GAA	ACAGGAAA	UUUCCUGUA	UGGAGGAA
	3914	CAUAAUGG	CUGAUGA	X	GAA	AUUUGGGG	CCCCAAAUU	CCAUUAUG
	3915	UCAUAAUG	CUGAUGA	X	GAA	AAUUUGGG	CCCAAAUUC	CAUUAUGA
	3919	GUUGUCAU	CUGAUGA	Х	GAA	AUGGAAUU	AAUUCCAUU	AUGACAAC
	3920	UGUUGUCA	CUGAUGA	Х	GAA	AAUGGAAU	AUUCCAUUA	UGACAACA
20	3939	UAAUGACU	CUGAUGA	Х	GAA	AUUCCUGC	GCAGGAAUC	AGUCAUUA
	3943	GAGAUAAU	CUGAUGA	Х	GAA	ACUGAUUC	GAAUCAGUC	AUUAUCUC
	3946	CUGGAGAU	CUGAUGA	Х	GAA	AUGACUGA	UCAGUCAUU	AUCUCCAG
	3947	UCUGGAGA	CUGAUGA	Х	GAA	AAUGACUG	CAGUCAUUA	UCUCCAGA
	3949	GUUCUGGA	CUGAUGA	x	GAA	AUAAUGAC	GUCAUUAUC	UCCAGAAC
25	3951	CUGUUCUG	CUGAUGA	X	GAA	AGAUAAUG	CAUUAUCUC	CAGAACAG
	3961	CUUUCGCU	CUGAUGA	X	GAA	ACUGUUCU	AGAACAGUA	AGCGAAAG
	3987	AAUGUUUU	CUGAUGA	Х	GAA	ACACUCAC	GUGAGUGUA	AAAACAUU
	3995	UAUCUUCA	CUGAUGA	х	GAA	AUGUUUUU	AAAAACAUU	UGAAGAUA
	3996	AUAUCUUC	CUGAUGA	X	GAA	AAUGUUUU	AAAACAUUU	GAAGAUAU
30	4003	CAAUGGGA	CUGAUGA	X	GAA	AUCUUCAA	UUGAAGAUA	UCCCAUUG

								• .
	4005	UCCAAUG	G CUGAUGA	λ >	GAA	A AUAUCUUC	GAAGAUAUC	CCAUUGGA
	4010	GUUCCUC	C CUGAUGA	A X	GAA	AUGGGAUA	UAUCCCAUU	GGAGGAAC
	4026	AUCACUU	J CUGAUGA	X	GAA	ACUUCUGG	CCAGAAGUA	AAAGUGAU
	4035	UCAUCUGO	G CUGAUGA	X	GAA	AUCACUUU	AAAGUGAUC	CCAGAUGA
5	4068	GAUGCAAC	CUGAUGA	X	GAA	ACCAUCCC	GGGAUGGUC	CUUGCAUC
	4071	UCUGAUGO	C CUGAUGA	X	GAA	AGGACCAU	AUGGUCCUU	GCAUCAGA
	4076	GCUCUUCU	J CUGAUGA	X	GAA	AUGCAAGG	CCUUGCAUC	AGAAGAGC
	4093	GUCUUCCA	CUGAUGA	X	GAA	AGUUUUCA	UGAAAACUC	UGGAAGAC
	4112	AUGGAGAU	J CUGAUGA	. x	GAA	AUUUGUUC	GAACAAAUU	AUCUCCAU
10	4113	GAUGGAGA	CUGAUGA	. X	GAA	AAUUUGUU	AACAAAUUA	UCUCCAUC
	4115	AAGAUGGA	CUGAUGA	X	GAA	AUAAUUUG	CAAAUUAUC	UCCAUCUU
	4117	AAAAGAUG	CUGAUGA	X	GAA	AGAUAAUU	AAUUAUCUC	CAUCUUUU
	4121	CACCAAAA	CUGAUGA	X	GAA	AUGGAGAU	AUCUCCAUC	UUUUGGUG
	4123	UCCACCAA	CUGAUGA	Х	GAA	AGAUGGAG	CUCCAUCUU	UUGGUGGA
15	4124	UUCCACCA	CUGAUGA	X	GAA	AAGAUGGA	UCCAUCUUU	UGGUGGAA
	4125	AUUCCACC	CUGAUGA	X	GAA	AAAGAUGG	CCAUCUUUU	GGUGGAAU []
	4144	CCUGCUUU	CUGAUGA	X	GAA	ACUGGGCA	UGCCCAGUA	AAAGCAGG "
	4157	AGGCCACA	CUGAUGA	X	GAA	ACUCCCUG	CAGGGAGUC	UGUGGCCU
	4166	AGCCUUCC	CUGAUGA	X	GAA	AGGCCACA	UGUGGCCUC	GGAAGGCU
20	4175	UCUGGUUG	CUGAUGA	Х	GAA	AGCCUUCC	GGAAGGCUC	CAACCAGA
	4193	CAGACUGG	CUGAUGA	X	GAA	AGCCACUG	CAGUGGCUA	CCAGUCUG
	4199	GAUACCCA	CUGAUGA	x	GAA	ACUGGUAG	CUACCAGUC	UGGGUAUC
	4205	CUGAGUGA	CUGAUGA	X	GAA	ACCCAGAC	GUCUGGGUA	UCACUCAG
	4207	AUCUGAGU	CUGAUGA	X	GAA	AUACCCAG	CUGGGUAUC	ACUCAGAU
25	4211	UGUCAUCU	CUGAUGA	X	GAA	AGUGAUAC	GUAUCACUC	AGAUGACA
	4235	CGCUGGAG	CUGAUGA	х	GAA	ACACGGUG	CACCGUGUA	CUCCAGCG
	4238	CGUCGCUG	CUGAUGA	Х	GAA	AGUACACG	CGUGUACUC	CAGCGACG
	4257	AUCUUUAA	CUGAUGA	X	GAA	AGUCCUGC	GCAGGACUU	UUAAAGAU
	4258	CAUCUUUA	CUGAUGA	X	GAA	AAGUCCUG	CAGGACUUU	UAAAGAUG
30	4259	CCAUCUUU	CUGAUGA	Х	GAA	AAAGUCCU	AGGACUUUU 2	AAAGAUGG

	4260	ACCAUCUU	CUGAUGA	X	GAA	AAAAGUCC	GGACUUUUA	AAGAUGGU
	4281	UCAGCGUG	CUGAUGA	X	GAA	ACUGCAGC	GCUGCAGUU	CACGCUGA
	4282	GUCAGCGU	CUGAUGA	Х	GAA	AACUGCAG	CUGCAGUUC	ACGCUGAC
	4292	UGGUCCCU	CUGAUGA	Х	GAA	AGUCAGCG	CGCUGACUC	AGGGACCA
5	4311	CAGGAGGU	CUGAUGA	X	GAA	AGCUGCAG	CUGCAGCUC	ACCUCCUG
	4316	UUAAACAG	CUGAUGA	X	GAA	AGGUGAGC	GCUCACCUC	CUGUUUAA
	4321	UCCAUUUA	CUGAUGA	Х	GAA	ACAGGAGG	CCUCCUGUU	UAAAUGGA
	4322	UUCCAUUU	CUGAUGA	X	GAA	AACAGGAG	CUCCUGUUU	AAAUGGAA
	4323	CUUCCAUU	CUGAUGA	X	GAA	AAACAGGA	UCCUGUUUA	AAUGGAAG
10	4336	CGGGACAG	CUGAUGA	Х	GAA	ACCACUUC	GAAGUGGUC	CUGUCCCG
	4341	GGAGCCGG	CUGAUGA	X	GAA	ACAGGACC	GGUCCUGUC	CCGGCUCC
	4348	UGGGGGCG	CUGAUGA	Х	GAA	AGCCGGGA	UCCCGGCUC	CGCCCCCA
	4360	AUUUCCAG	CUGAUGA	X	GAA	AGUUGGGG	CCCCAACUC	CUGGAAAU
	4369	ucucucgu	CUGAUGA	Х	GAA	AUUUCCAG	CUGGAAAUC	ACGAGAGA
15	4387	GAAAAUCU	CUGAUGA	X	GAA	AGCAGCAC	GUGCUGCUU	AGAUUUUC
	4388	UGAAAAUC	CUGAUGA	X	GAA	AAGCAGCA	UGCUGCUUA	GAUUUUCA
	4392	CACUUGAA	CUGAUGA	Х	GAA	AUCUAAGC	GCUUAGAUU	UUCAAGUG
	4393	ACACUUGA	CUGAUGA	Χ	GAA	AAUCUAAG	CUUAGAUUU	UCAAGUGU
	4394	AACACUUG	CUGAUGA	X	GAA	AAAUCUAA	UUAGAUUUU	CAAGUGUU
20	4395	CAACACUU	CUGAUGA	Х	GAA	AAAAUCUA	UAGAUUUUC	AAGUGUUG
	4402	GAAAGAAC	CUGAUGA	X	GAA	ACACUUGA	UCAAGUGUU	GUUCUUUC
	4405	GUGGAAAG	CUGAUGA	X	GAA	ACAACACU	AGUGUUGUU	CUUUCCAC
	4406	GGUGGAAA	CUGAUGA	X	GAA	AACAACAC	GUGUUGUUC	UUUCCACC
	4408	GUGGUGGA	CUGAUGA	X	GAA	AGAACAAC	GUUGUUCUU	UCCACCAC
25	4409	GGUGGUGG	CUGAUGA	X	GAA	AAGAACAA	UUGUUCUUU	CCACCACC
	4410	GGGUGGUG	CUGAUGA	X	GAA	AAAGAACA	UGUUCUUUC	CACCACCC
	4425	AAUGUGGC	CUGAUGA	X	GAA	ACUUCCGG	CCGGAAGUA	GCCACAUU
	4433	GAAAAUCA	CUGAUGA	Х	GAA	AUGUGGCU	AGCCACAUU	UGAUUUUC
	4434	UGAAAAUC	CUGAUGA	X	GAA	AAUGUGGC	GCCACAUUU	GAUUUUCA
30	4438	AAAAUGAA	CUGAUGA	X	GAA	AUCAAAUG	CAUUUGAUU	UUCAUUUU

় - নুর্

	4439	AAAAAUGA	CUGAUGA	. >	GA.	AAUCAAAU	AUUUGAUU	UCAUUUUU .
	4440	CAAAAAUG	CUGAUGA	. }	GA	AAAUCAAA	UUUGAUUUL	CAUUUUUG
	4441	CCAAAAAU	CUGAUGA	. X	GAA	AAAAUCAA	UUGAUUUUC	: AUUUUUGG
	4444	CCUCCAAA	CUGAUGA	. X	GAA	AUGAAAAU	AUUUUCAUU	UUUGGAGG
5	4445	UCCUCCAA	CUGAUGA	. X	GAA	AAUGAAAA	UUUUCAUUU	UUGGAGGA
	4446	CUCCUCCA	CUGAUGA	X	GAA	AAAUGAAA	UUUCAUUUU	UGGAGGAG
	4447	CCUCCUCC	CUGAUGA	X	GAA	AAAAUGAA	UUCAUUUUU	GGAGGAGG
	4461	UGCAGUCU	CUGAUGA	X	GAA	AGGUCCCU	AGGGACCUC	AGACUGCA
	4477	CUGAGGAC	CUGAUGA	X	GAA	AGCUCCUU	AAGGAGCUU	GUCCUCAG
10	4480	GCCCUGAG	CUGAUGA	Х	GAA	ACAAGCUC	GAGCUUGUC	CUCAGGGC
	4483	AAUGCCCU	CUGAUGA	Х	GAA	AGGACAAG	CUUGUCCUC	AGGGCAUU
	4491	UCUCUGGA	CUGAUGA	X	GAA	AUGCCCUG	CAGGGCAUU	UCCAGAGA
	4492	UUCUCUGG	CUGAUGA	X	GAA	AAUGCCCU	AGGGCAUUU	CCAGAGAA
	4493	CUUCUCUG	CUGAUGA	Х	GAA	AAAUGCCC	GGGCAUUUC	CAGAGAAG
15	452 5	GUAGAGUC	CUGAUGA	Х	GAA	ACACAUUC	GAAUGUGUU	GACUCUAC
	4530	AGAGAGUA	CUGAUGA	X	GAA	AGUCAACA	UGUUGACUC	UACUCUCU
	4532	AAAGAGAG	CUGAUGA	X	GAA	AGAGUCAA	UUGACUCUA	CUCUCUUU
	4535	GGAAAAGA	CUGAUGA	X	GAA	AGUAGAGU	ACUCUACUC	ncnnncc
	4537	AUGGAAAA	CUGAUGA	X	GAA	AGAGUAGA	UCUACUCUC	UUUUCCAU
20	4539	GAAUGGAA	CUGAUGA	Х	GAA	AGAGAGUA	UACUCUCUU	UUCCAUUC
	4540	UGAAUGGA	CUGAUGA	X	GAA	AAGAGAGU	ACUCUCUUU	UCCAUUCA
	4541	AUGAAUGG	CUGAUGA	X	GAA	AAAGAGAG	cucucuuuu	CCAUUCAU
	4542	AAUGAAUG	CUGAUGA	Х	GAA	AAAAGAGA	ucucuuuuc	CAUUCAUU
	4546	UUUAAAUG	CUGAUGA	X	GAA	AUGGAAAA	UUUUCCAUU	CAUUUAAA
25	4547	UUUUAAAU	CUGAUGA	X	GAA	AAUGGAAA	UUUCCAUUC	AUUUAAAA
	4550	GACUUUUA	CUGAUGA	X	GAA	AUGAAUGG	CCAUUCAUU	UAAAAGUC
	4551	GGACUUUU	CUGAUGA	X	GAA	AAUGAAUG	CAUUCAUUU	AAAAGUCC
	4552	AGGACUUU	CUGAUGA	X	GAA	AAAUGAAU	AUUCAUUUA	AAAGUCCU
	4558	UUAUAUAG	CUGAUGA	X	GAA	ACUUUUAA	UUAAAAGUC	CUAUAUAA
30	4561	ACAUUAUA	CUGAUGA	Х	GAA	AGGACUUU	AAAGUCCUA	UAUAAUGU

	4563	GCACAUUA	CUGAUGA	X	GAA	AUAGGACU	AGUCCUAUA	UAAUGUGC
	4565	GGGCACAU	CUGAUGA	X	GAA	AUAUAGGA	UCCUAUAUA	AUGUGCCC
	4583	GGUAGUGA	CUGAUGA	Х	GAA	ACCACAGC	GCUGUGGUC	UCACUACC
	4585	CUGGUAGU	CUGAUGA	X	GAA	AGACCACA	UGUGGUCUC	ACUACCAG
5	4589	UUAACUGG	CUGAUGA	Х	GAA	AGUGAGAC	GUCUCACUA	CCAGUUAA
	4595	UUUGCUUU	CUGAUGA	Х	GAA	ACUGGUAG	CUACCAGUU	AAAGCAAA
	4596	UUUUGCUU	CUGAUGA	Х	GAA	AACUGGUA	UACCAGUUA	AAGCAAAA
	4609	GUGUUUGA	CUGAUGA	Х	GAA	AGUCUUUU	AAAAGACUU	UCAAACAC
	4610	CGUGUUUG	CUGAUGA	X	GAA	AAGUCUUU	AAAGACUUU	CAAACACG
10	4611	ACGUGUUU	CUGAUGA	Х	GAA	AAAGUCUU	AAGACUUUC	AAACACGU
	4625	GGAGGACA	CUGAUGA	X	GAA	AGUCCACG	CGUGGACUC	UGUCCUCC
	4629	UCUUGGAG	CUGAUGA	Х	GAA	ACAGAGUC	GACUCUGUC	CUCCAAGA
	4632	ACUUCUUG	CUGAUGA	х	GAA	AGGACAGA	UCUGUCCUC	CAAGAAGU
	4654	GUUUCACA	CUGAUGA	Х	GAA	AGGUGCCG	CGGCACCUC	UGUGAAAC
15	4668	GCCCAUUC	CUGAUGA	Х	GAA	AUCCAGUU	AACUGGAUC	GAAUGGGC
	46 83	AACACACA	CUGAUGA	X	GAA	AGCAUUGC	GCAAUGCUU	uguguguu
	4684	CAACACAC	CUGAUGA	Х	GAA	AAGCAUUG	CAAUGCUUU	GUGUGUUG
	4691	CCAUCCUC	CUGAUGA	Х	GAA	ACACACAA	UUGUGUGUU	GAGGAUGG
	4709	GGCCCUGG	CUGAUGA	Х	GAA	ACAUCUCA	UGAGAUGUC	CCAGGGCC
20	4722	GGUAGACA	CUGAUGA	Х	GAA	ACUCGGCC	GGCCGAGUC	UGUCUACC
	4726	CCAAGGUA	CUGAUGA	X	GAA	ACAGACUC	GAGUCUGUC	UACCUUGG
	4728	CUCCAAGG	CUGAUGA	X	GAA	AGACAGAC	GUCUGUCUA	CCUUGGAG
	4732	AAGCCUCC	CUGAUGA	X	GAA	AGGUAGAC	GUCUACCUU	GGAGGCUU
	4740	CCUCCACA	CUGAUGA	X	GAA	AGCCUCCA	UGGAGGCUU	UGUGGAGG
25	4741	UCCUCCAC	CUGAUGA	Х	GAA	AAGCCUCC	GGAGGCUUU	GUGGAGGA
	4758	UUGGCUCA	CUGAUGA	X	GAA	AGCCCGCA	UGCGGGCUA	UGAGCCAA
	4771	CCACACUU	CUGAUGA	X	GAA	ACACUUGG	CCAAGUGUU	AAGUGUGG
	4772	CCCACACU	CUGAUGA	X	GAA	AACACUUG	CAAGUGUUA	AGUGUGGG
	4811	CUCCGAGC	CUGAUGA	Х	GAA	ACUUGCGC	GCGCAAGUC	GCUCGGAG
30	4815	CGCUCUCC	CUGAUGA	X	GAA	AGCGACUU	AAGUCGCUC	GGAGAGCG

. . .

**

	4826 CAGGCUCC CUGAUGA X GAA ACCGCUCU	AGAGCGGUU GGAGCCUG
	4844 GCCAGCAC CUGAUGA X GAA AUGCAUCU	AGAUGCAUU GUGCUGGC
	4854 CUCCACCA CUGAUGA X GAA AGCCAGCA	UGCUGGCUC UGGUGGAG
	4870 CAGGCCAC CUGAUGA X GAA AGCCCACC	GGUGGGCUU GUGGCCUG
5	4880 CGUUUCCU CUGAUGA X GAA ACAGGCCA	UGGCCUGUC AGGAAACG
	4908 CAAAACCA CUGAUGA X GAA ACCCUGCC	GGCAGGGUU UGGUUUUG
	4909 CCAAAACC CUGAUGA X GAA AACCCUGC	GCAGGGUUU GGUUUUGG
	4913 CCUUCCAA CUGAUGA X GAA ACCAAACC	GGUUUGGUU UUGGAAGG
	4914 ACCUUCCA CUGAUGA X GAA AACCAAAC	GUUUGGUUU UGGAAGGU
10	4915 AACCUUCC CUGAUGA X GAA AAACCAAA	UUUGGUUUU GGAAGGUU
	4923 AGCACGCA CUGAUGA X GAA ACCUUCCA	UGGAAGGUU UGCGUGCU
	4924 GAGCACGC CUGAUGA X GAA AACCUUCC	GGAAGGUUU GCGUGCUC
	4932 ACUGUGAA CUGAUGA X GAA AGCACGCA	UGCGUGCUC UUCACAGU
	4934 CGACUGUG CUGAUGA X GAA AGAGCACG	CGUGCUCUU CACAGUCG
15	4935 CCGACUGU CUGAUGA X GAA AAGAGCAC	
	4941 UGUAACCC CUGAUGA X GAA ACUGUGAA	UUCACAGUC GGGUUACA
	4946 UCGCCUGU CUGAUGA X GAA ACCCGACU	AGUCGGGUU ACAGGCGA
	4947 CUCGCCUG CUGAUGA X GAA AACCCGAC	GUCGGGUUA CAGGCGAG
	4957 CCACAGGG CUGAUGA X GAA ACUCGCCU	AGGCGAGUU CCCUGUGG
20	4958 GCCACAGG CUGAUGA X GAA AACUCGCC	GGCGAGUUC CCUGUGGC
	4969 GAGUAGGA CUGAUGA X GAA ACGCCACA	UGUGGCGUU UCCUACUC
		GUGGCGUUU CCUACUCC
	4971 AGGAGUAG CUGAUGA X GAA AAACGCCA	UGGCGUUUC CUACUCCU
	4974 AUUAGGAG CUGAUGA X GAA AGGAAACG	CGUUUCCUA CUCCUAAU
25	4977 CUCAUUAG CUGAUGA X GAA AGUAGGAA	UUCCUACUC CUAAUGAG
	4980 ACUCUCAU CUGAUGA X GAA AGGAGUAG	CUACUCCUA AUGAGAGU
	4989 CCGGAAGG CUGAUGA X GAA ACUCUCAU	AUGAGAGUU CCUUCCGG
	4990 UCCGGAAG CUGAUGA X GAA AACUCUCA	UGAGAGUUC CUUCCGGA
	4993 GAGUCCGG CUGAUGA X GAA AGGAACUC	GAGUUCCUU CCGGACUC
30	4994 AGAGUCCG CUGAUGA X GAA AAGGAACU	AGUUCCUUC CGGACUCU

	5001	ACACGUAA	CUGAUGA	Х	GAA	AGUCCGGA	UCCGGACUC	UUACGUGU
	5003	AGACACGU	CUGAUGA	X	GAA	AGAGUCCG	CGGACUCUU	ACGUGUCU
	5004	GAGACACG	CUGAUGA	X	GAA	AAGAGUCC	GGACUCUUA	CGUGUCUC
	5010	GGCCAGGA	CUGAUGA	Х	GAA	ACACGUAA	UUACGUGUC	UCCUGGCC
5	5012	CAGGCCAG	CUGAUGA	X	GAA	AGACACGU	ACGUGUCUC	CUGGCCUG
	5046	GAAGGAGC	CUGAUGA	X	GAA	AGCUGCAU	AUGCAGCUU	GCUCCUUC
	5050	UGAGGAAG	CUGAUGA	X	GAA	AGCAAGCU	AGCUUGCUC	CUUCCUCA
	5053	AGAUGAGG	CUGAUGA	Х	GAA	AGGAGCAA	UUGCUCCUU	CCUCAUCU
	5054	GAGAUGAG	CUGAUGA	Х	GAA	AAGGAGCA	UGCUCCUUC	CUCAUCUC
10	5057	UGAGAGAU	CUGAUGA	Х	GAA	AGGAAGGA	uccuuccuc	AUCUCUCA
	5060	GCCUGAGA	CUGAUGA	X	GAA	AUGAGGAA	UUCCUCAUC	UCUCAGGC
	5062	CAGCCUGA	CUGAUGA	Х	GAA	AGAUGAGG	CCUCAUCUC	UCAGGCUG
	5064	CACAGCCU	CUGAUGA	Х	GAA	AGAGAUGA	UCAUCUCUC	AGGCUGUG
	5076	UCUGAAUU	CUGAUGA	Х	GAA	AGGCACAG	CUGUGCCUU	AAUUCAGA
15	5077	UUCUGAAU	CUGAUGA	X	GAA	AAGGCACA	UGUGCCUUA	AUUCAGAA
	5080	GUGUUCUG	CUGAUGA	X	GAA	AUUAAGGC	GCCUUAAUU	CAGAACAC
	5081	GGUGUUCU	CUGAUGA	X	GAA	AAUUAAGG	CCUUAAUUC	AGAACACC
	5105	CCUCUGCC	CUGAUGA	X	GAA	ACGUUCCU	AGGAACGUC	GGCAGAGG
	5116	CCCGUCAG	CUGAUGA	Х	GAA	AGCCUCUG	CAGAGGCUC	CUGACGGG
20	5135	GUUCUCAC	CUGAUGA	Х	GAA	AUUCUUCG	CGAAGAAUU	GUGAGAAC
	5156	GAAACCCU	CUGAUGA	Х	GAA	AGUUUCUG	CAGAAACUC	AGGGUUUC
	5162	CCAGCAGA	CUGAUGA	X	GAA	ACCCUGAG	CUCAGGGUU	UCUGCUGG
	51 63	CCCAGCAG	CUGAUGA	Х	GAA	AACCCUGA	UCAGGGUUU	CUGCUGGG
	5164	ACCCAGCA	CUGAUGA	X	GAA	AAACCCUG	CAGGGUUUC	UGCUGGGU
25	5203	AACCCUCA	CUGAUGA	X	GAA	ACCUGCCA	UGGCAGGUC	UGAGGGUU
	5211	UGACAGAG	CUGAUGA	Х	GAA	ACCCUCAG	CUGAGGGUU	CUCUGUCA
	5212	UUGACAGA	CUGAUGA	х	GAA	AACCCUCA	UGAGGGUUC	UCUGUCAA
	5214	ACUUGACA	CUGAUGA	Х	GAA	AGAACCCU	AGGGUUCUC	UGUCAAGU
	5218	CGCCACUU	CUGAUGA	Х	GAA	ACAGAGAA	UUCUCUGUC	AAGUGGCG
30	5229	UGAGCCUU	CUGAUGA	Х	GAA	ACCGCCAC	GUGGCGGUA	AAGGCUCA

湯

	5236 ACCAGCCU CUGAUGA X GAA AGCCUUUA	UAAAGGCUC AGGCUGGU
	5247 AGAGGAAG CUGAUGA X GAA ACACCAGC	GCUGGUGUU CUUCCUCU
	5248 UAGAGGAA CUGAUGA X GAA AACACCAG	CUGGUGUUC UUCCUCUA
	5250 GAUAGAGG CUGAUGA X GAA AGAACACC	GGUGUUCUU CCUCUAUC
5	5251 AGAUAGAG CUGAUGA X GAA AAGAACAC	GUGUUCUUC CUCUAUCU
	5254 UGGAGAUA CUGAUGA X GAA AGGAAGAA	UUCUUCCUC UAUCUCCA
	5256 AGUGGAGA CUGAUGA X GAA AGAGGAAG	CUUCCUCUA UCUCCACU
	5258 GGAGUGGA CUGAUGA X GAA AUAGAGGA	UCCUCUAUC UCCACUCC
	5260 CAGGAGUG CUGAUGA X GAA AGAUAGAG	CUCUAUCUC CACUCCUG
10	5265 CCUGACAG CUGAUGA X GAA AGUGGAGA	UCUCCACUC CUGUCAGG
	5270 GGGGGCCU CUGAUGA X GAA ACAGGAGU	ACUCCUGUC AGGCCCCC
	5283 AUACUGAG CUGAUGA X GAA ACUUGGGG	CCCCAAGUC CUCAGUAU
	5286 AAAAUACU CUGAUGA X GAA AGGACUUG	CAAGUCCUC AGUAUUUU
	5290 AGCUAAAA CUGAUGA X GAA ACUGAGGA	UCCUCAGUA UUUUAGCU
15	5292 AAAGCUAA CUGAUGA X GAA AUACUGAG	CUCAGUAUU UUAGCUUU
	5293 CAAAGCUA CUGAUGA X GAA AAUACUGA	UCAGUAUUU UAGCUUUG
	5294 ACAAAGCU CUGAUGA X GAA AAAUACUG	CAGUAUUUU AGCUUUGU
	5295 CACAAAGC CUGAUGA X GAA AAAAUACU	AGUAUUUUA GCUUUGUG
	5299 AAGCCACA CUGAUGA X GAA AGCUAAAA	UUUUAGCUU UGUGGCUU
20	5300 GAAGCCAC CUGAUGA X GAA AAGCUAAA	
	5307 CCAUCAGG CUGAUGA X GAA AGCCACAA	UUGUGGCUU CCUGAUGG
	5308 GCCAUCAG CUGAUGA X GAA AAGCCACA	UGUGGCUUC CUGAUGGC
	5325 CCAAUUAA CUGAUGA X GAA AUUUUUCU	AGAAAAAUC UUAAUUGG
		AAAAAUCUU AAUUGGUU
25		AAAAUCUUA AUUGGUUG
		AUCUUAAUU GGUUGGUU
		UAAUUGGUU GGUUUGCU
		UGGUUGGUU UGCUCUCC
		GGUUGGUUU GCUCUCCA
30	5344 UAUCUGGA CUGAUGA X GAA AGCAAACC	GGUUUGCUC UCCAGAUA

	5346	AUUAUCUG	CUGAUGA	X	GAA	AGAGCAAA	UUUGCUCUC	CAGAUAAU
	5352	CUAGUGAU	CUGAUGA	Х	GAA	AUCUGGAG	CUCCAGAUA	AUCACUAG
	5355	UGGCUAGU	CUGAUGA	X	GAA	AUUAUCUG	CAGAUAAUC	ACUAGCCA
	5359	AAUCUGGC	CUGAUGA	X	GAA	AGUGAUUA	UAAUCACUA	GCCAGAUU
5	5367	AAUUUCGA	CUGAUGA	Х	GAA	AUCUGGCU	AGCCAGAUU	UCGAAAUU
	5368	UAAUUUCG	CUGAUGA	X	GAA	AAUCUGGC	GCCAGAUUU	CGAAAUUA
	5369	GUAAUUUC	CUGAUGA	Х	GAA	AAAUCUGG	CCAGAUUUC	GAAAUUAC
	5375	UAAAAAGU	CUGAUGA	X	GAA	AUUUCGAA	UUCGAAAUU	ACUUUUUA
	5376	CUAAAAAG	CUGAUGA	Х	GAA	AAUUUCGA	UCGAAAUUA	CUUUUUAG
10	5379	CGGCUAAA	CUGAUGA	X	GAA	AGUAAUUU	AAAUUACUU	UUUAGCCG
	5380	UCGGCUAA	CUGAUGA	Х	GAA	AAGUAAUU	AAUUACUUU	UUAGCCGA
	5381	CUCGGCUA	CUGAUGA	Х	GAA	AAAGUAAU	AUUACUUUU	UAGCCGAG
	5382	CCUCGGCU	CUGAUGA	Х	GAA	AAAAGUAA	UUACUUUUU	AGCCGAGG
	5383	ACCUCGGC	CUGAUGA	Х	GAA	AAAAAGUA	UACUUUUUA	GCCGAGGU
15	5392	GUUAUCAU	CUGAUGA	X	GAA	ACCUCGGC	GCCGAGGUU	AUGAUAAC
	5393	UGUUAUCA	CUGAUGA	Х	GAA	AACCUCGG	CCGAGGUUA	UGAUAACA
	5398	GUAGAU GU	CUGAUGA	X	GAA	AUCAUAAC	GUUAUGAUA	ACAUCUAC
	5403	AUACAGUA	CUGAUGA	Χ	GAA	AUGUUAUC	GAUAACAUC	UACUGUAU
	5405	GGAUACAG	CUGAUGA	X	GAA	AGAUGUUA	UAACAUCUA	CUGUAUCC
20	5410	CUAAAGGA	CUGAUGA	Χ	GAA	ACAGUAGA	UCUACUGUA	UCCUUUAG
	5412	UUCUAAAG	CUGAUGA	X	GAA	AUACAGUA	UACUGUAUC	CUUUAGAA
	5415	AAAUUCUA	CUGAUGA	Х	GAA	AGGAUACA	UGUAUCCUU	UAGAAUUU
	5416	AAAAUUCU	CUGAUGA	Х	GAA	AAGGAUAC	GUAUCCUUU	AGAAUUUU
	5417	UAAAAUUC	CUGAUGA	Х	GAA	AAAGGAUA	UAUCCUUUA	GAAUUUUA
25	5422	UAGGUUAA	CUGAUGA	Х	GAA	AUUCUAAA	UUUAGAAUU	UUAACCUA
	5423	AUAGGUUA	CUGAUGA	X	GAA	AAUUCUAA	UUAGAAUUU	UAACCUAU
	5424	UAUAGGUU	CUGAUGA	Х	GAA	AAAUUCUA	UAGAAUUUU	AACCUAUA
	5425	UUAUAGGU	CUGAUGA	X	GAA	AAAAUUCU	AGAAUUUUA	ACCUAUAA
	5430	UAGUUUUA	CUGAUGA	X	GAA	AGGUUAAA	UUUAACCUA	UAAAACUA
30	5432	CAUAGUUU	CUGAUGA	Х	GAA	AUAGGUUA	UAACCUAUA	AAACUAUG

	5438	AGUAGACA	CUGAUGA	X	GAA	AGUUUUAU	AUAAAACUA	UGUCUACU
	5442	AACCAGUA	CUGAUGA	х	GAA	ACAUAGUU	AACUAUGUC	UACUGGUU
	5444	GAAACCAG	CUGAUGA	X	GAA	AGACAUAG	CUAUGUCUA	CUGGUUUC
	5450	CAGGCAGA	CUGAUGA	Х	GAA	ACCAGUAG	CUACUGGUU	UCUGCCUG
5	5451	ACAGGCAG	CUGAUGA	х	GAA	AACCAGUA	UACUGGUUU	CUGCCUGU
	5452	CACAGGCA	CUGAUGA	х	GAA	AAACCAGU	ACUGGUUUC	UGCCUGUG

Where "X" represents stem II region of a HH ribozyme (Hertel et al., 1992 $Nucleic\ Acids\ Res.\ 20\ 3252$). The length of stem II may be \ge 2 base-pairs.

150

Table VII: Mouse flk-1 VEGF Recentor-Hairpin Ribozyme and Substrate Sequences

	Table	<u> Table VII: Mouse fik-l VEGF Receptor-Hairpin Kibozyme and Substrate Sequences</u>	eduences
	nt.	HP Ribozyme Sequence	Substrate
	Posi-		
	tion		
5	74	GGGACACA AGAA GGGCCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	GGGCCCA GAC UGUGUCCC
	88	GUUAUCCC AGAA GCGGGA ACCAGAGAAACACGCUGUGGUACAUUACCUGGUA	UCCCGCA GCC GGGAUAAC
	105	GGAAUCGG AGAA GCCAGG ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	ccusacu sac cesauuce
	110	UCCGCGGA AGAA GGUCAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CUGACCC GAU UCCGCGGA
	125	CGGCUGUC AGAA GUGUCC ACCAGAGAAACACGCUUGUGGUACAUUACCUGGUA	GGACACC GCU GACAGCCG
10	132	CCAGCCGC AGAA GUCAGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GCUGACA GCC GCGGCUGG
	138	CUGGCUCC AGAA GCGGCU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	AGCCGCG GCU GGAGCCAG
	175	CAGCGCAA AGAA GGGGAG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	ancecee ene aneceene
	199	GUCACAGA AGAA GUAUGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CCAUACC GCC UCUGUGAC
	309	CACAGAGC AGAA GCUAGC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	GCUAGCU GUC GCUCUGUG
15	342	CCCACAGA AGAA GCUCGG ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CCGAGCC GCC UCUGUGGG
	434	UGCAAGUA AGAA GAAGGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	cccuuca gau uacuugca
	630	UAGACAUA AGAA GUGGAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CUCCACU GUU UAUGUCUA
	655	GAAUGGUG AGAA GUAAUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GAUUACA GAU CACCAUUC
	739	CGACCCUC AGAA GGGGAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	AUCCCCU GCC GAGGGUCG

UCCUACG GAC CGUUAAGC

GCUUAACG AGAA GUAGGA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA

								151									
UGUUCCG GAU GGAAACAG	CCUAUCA GUC UAUCAUGU	GCUAUCU GCC GGAGAAAA	GUGGACG GAU GAUCAAGA	UNACCCA GCU CCUGAUAU	CACCCCA GAU CGGUGAGA	AUGCACA GUC UACGCCAA	GAAGCCU GCU CCUACAGA	UCCUACA GAC CCGGCCAA	AUGCCCU GAU UGAAGGAA	GCAACCU GCU GCCCAGCC	ACCUGCU GCC CAGCCAAC	Dence on enecyclic	AACAUCG GUC CACAUGGG	CACACCA GUU UGCAAGAA	UUGCUCU GCU CAAGAIIAA	UCAAACA GCU CAUCAIICC	GGAACCU GAC UAUCCGCA
CUGUTUCC AGAA GGAACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	ACAUGAUA AGAA GAUAGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UNUUCUCC AGAA GAUAGC ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UCUUGAUC AGAA GUCCAC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	AUAUCAGG AGAA GGGUAA	UCUCACCG AGAA GGGGUG	UUGGCGUA AGAA GUGCAU ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UCUGUAGG AGAA GGCUUC ACCAGAGAAACACGCUUGUGGUACAUUACCUGGUA	UUGGCCGG AGAA GUAGGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UUCCUUCA AGAA GGGCAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GGCUGGGC AGAA GGUUGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GUUGGCUG AGAA GCAGGU	CAGUGCAC AGAA GGGACA	CCCAUGUG AGAA GAUGUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UUCUUGCA AGAA GGUGUG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UVAUCUUG AGAA GAGCAA	GGAUGAUG AGAA GUUUGA	UGCGGAUA AGAA GGUUCC
807	920	1002	1229	5 1365	1556	1629	1687	1696	1796	1950	1953	1985	2055	2082	2208	2252	2444
				u i					10					15			

UGCUGCA GUU CACGCUGA

GCAGCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

UCAGCGUG AGAA

4278

15

152 GGAUCCA GAU GAAUUGCC GAAACUAG GCUUUUGG GCU CAGGCUUU ACUUCCU GAC CUUGGAGC UGUUACA GCU UCCAAGUG AGACCCG GAU UAUGUCAG GAUGECE GAE UECEUTUG BCU UGGCCCGG GGCUCCU GAC UACACUAC UGUACCA GAC CAUGCUGG CUGGACU GCU GGCAUGAG UCUCCCU GCC UACCUCAC CUCACCU GUU UCCUGUAU GAUCCCA GAU GACAGCCA CAGUGGCU GCUACCA GUC UGGGUAUC UCACUCA GAU GACACAGA GCU GAC CCAACCA GAC GGGACCG UGAGGCA GACUUCG UCUGCCA GCCAAUUC AGAA GGAUCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGCAGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCCUCA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA SCUCCAAG AGAA GGAAGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUAACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAAGUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CUGACAUA AGAA GGGUCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CAAAGGGA AGAA GGCAUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA SUAGUGUA AGAA GGAGCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CCAGCAUG AGAA GGUACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CUCAUGCC AGAA GUCCAG ACCAGAGAAACACGGUUGUGGUACAUUACCUGGUA GGGAGA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA AUACAGGA AGAA GGUGAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGAUC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA SAUACCCA AGAA GGUAGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAGUGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGUCCC GGUUGG AGAA CCAAAAGC AGAA AAAGCCUG AGAA CACUUGGA AGAA AGAA GUGAGGUA AGAA UCUGUGUC AGAA UGGCUGUC AGAA AGCCACUG AGAA CUAGUUUC CCGGGCCA 2703 2777 2832 3199 3278 3304 3450 3475 3689 3860 3421 3663 3703 3873 4038 4196 4212 4181

10

BNSDOCID: <WO 9715662A2_I_:

S

153 UCACGCU GAC UCAGGGAC CCGGCNCC CACUGCA GCU CACCUCCU ACCUCCU GUU UAAAUGGA UGUCCCG GCU CCGCCCCC CGGCUCC GCC CCCAACUC AGGUGCU GCU UAGAUUUU GGACUCU GUC CUCCAAGA UGCAAGGA CUGGUCUC CGAGUCU GUC UACCUUGG GGAGCCUG GCCUGCA GAU GCAUUGUG GGCAGGGU CUUCACA GUC GGGUUACA GGUUUCU GCU GGGUGGAG CCUUCCG GAC UCUUACGU UGAUGCA GCU UGCUCCUU GGCUCCU GAC GGGGCCGA GACCUCA GAC UGGUCCU GUC eneceen een GAGAGCG GUU AAAGGCG GCC GUCCCUGA AGAA GCGUGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UCCAUTUA AGAA GGAGGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGAGCCGG AGAA GGACCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA GGGACA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GAGCCG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GCACCU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA UCCUUGCA AGAA GAGGUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAGACCAC AGAA GGGCAC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CCAAGGUA AGAA GACUCG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAGUCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CAGGCUCC AGAA GCUCUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CACAAUGC AGAA GCAGGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCCUUU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GUGAAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA ACGUAAGA AGAA GGAAGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCAUCA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGAGCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CUCCACCC AGAA GAAACC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCAGUG AGAA GGGGCGG AGAA GAGUUGGG AGAA AAAAUCUA AGAA UCUUGGAG AGAA ACCCUGCC AGAA AAGGAGCA AGAA UGUAACCC AGAA UCGGCCCC AGAA AGGAGGUG 4287 4307 4318 4338 4344 4349 4383 4462 4626 4836 4574 4723 4823 4938 4896 4996 5042 5118 5165

10

15

153

S

4	•
ù)
_	1

GENNACH GCC UGNGUGCH	AGCACACA AGAA GAAACC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	5453
CUAGCCA GAU UUCGAAAU	AUUUCGAA AGAA GGCUAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	5363
GCUUCCU GAU GGCAGAAA	UNUCUGUC AGAA GGAAGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	2310

155

Table VIII: Mouse flt-1 VEGF Receptor-Hammerhead Ribozyme and Substrate Sequence

	nt.		HH Riboz	ym	e Se	quence	Substrate
	Posi-						
5	tion						
	17	GUGAGCAA	CUGAUGA	X	GAA	ACGCGGCC	GGCCGCGUC UUGCUCAC
	19	UGGUGAGO	CUGAUGA	X	GAA	AGACGCGG	CCGCGUCUU GCUCACCA
	23	ACCAUGGU	CUGAUGA	Х	GAA	AGCAAGAC	GUCUUGCUC ACCAUGGU
	32	CAGCAGCU	CUGAUGA	х	GAA	ACCAUGGU	ACCAUGGUC AGCUGCUG
10	53	UAAGGCAA	CUGAUGA	Х	GAA	ACCGCGGU	ACCGCGGUC UUGCCUUA
	55	CGUAAGGC	CUGAUGA	х	GAA	AGACCGCG	CGCGGUCUU GCCUUACG
	60	CAGCGCGU	CUGAUGA	Х	GAA	AGGCAAGA	UCUUGCCUU ACGCGCUG
	61	GCAGCGCG	CUGAUGA	х	GAA	AAGGCAAG	CUUGCCUUA CGCGCUGC
	71	AGACACCC	CUGAUGA	X	GAA	AGCAGCGC	GCGCUGCUC GGGUGUCU
15	78	GAGAAGCA	CUGAUGA	X	GAA	ACACCCGA	ucggguguc ugcuucuc
	83	CCUGUGAG	CUGAUGA	X	GAA	AGCAGACA	UGUCUGCUU CUCACAGG
	84	UCCUGUGA	CUGAUGA	X	GAA	AAGCAGAC	GUCUGCUUC UCACAGGA
	86	UAUCCUGU	CUGAUGA	X	GAA	AGAAGCAG	CUGCUUCUC ACAGGAUA
	94	CUGAGCCA	CUGAUGA	Х	GAA	AUCCUGUG	CACAGGAUA UGGCUCAG
20	100	UCGACCCU	CUGAUGA	Х	GAA	AGCC AU AU	AUAUGGCUC AGGGUCGA
	106	UUAACUUC	CUGAUGA	X	GAA	ACCCUGAG	CUCAGGGUC GAAGUUAA
	112	GCACUUUU	CUGAUGA	X	GAA	ACUUCGAC	GUCGAAGUU AAAAGUGC
	113	GGCACUUU	CUGAUGA	X	GAA	AACUUCGA	UCGAAGUUA AAAGUGCC
	132	GCCUUUUA	CUGAUGA	X	GAA	ACUCAGUU	AACUGAGUU UAAAAGGC
25	133	UGCCUUUU	CUGAUGA	X	GAA	AACUCAGU	ACUGAGUUU AAAAGGCA
	134	GUGCCUUU	CUGAUGA	X	GAA	AAACUCAG	CUGAGUUUA AAAGGCAC
	152	GCUUGCAU	CUGAUGA	х	GAA	ACAUGCUG	CAGCAUGUC AUGCAAGC
	171	GAGAAAGA	CUGAUGA	Х	GAA	AGUCUGGC	GCCAGACUC UCUUUCUC
	173	UUGAGAAA	CUGAUGA	Х	GAA	AGAGUCUG	CAGACUCUC UUUCUCAA
30	175	ACUUGAGA	CUGAUGA	Х	GAA	AGAGAGUC	GACUCUCUU UCUCAAGU
	176	CACUUGAG	CUGAUGA	Х	GAA	AAGAGAGU	ACUCUCUUU CUCAAGUG
	177	GCACUUGA	CUGAUGA	Х	GAA	AAAGAGAG	CUCUCUUUC UCAAGUGC

	179	CUGCACUU	CUGAUGA	X	GAA	AGAAAGAG	cucuuucuc	AAGUGCAG
	205	GAGACCAU	CUGAUGA	Х	GAA	AGUGGGCU		AUGGUCUC
	211	UGGGCAGA	CUGAUGA	Х	GAA	ACCAUGAG	CUCAUGGUC	UCUGCCCA
	213	CGUGGGCA	CUGAUGA	Х	GAA	AGACCAUG	CAUGGUCUC	UGCCCACG
5	254	GGGGGAGU	CUGAUGA	X	GAA	AUGCUCAG	CUGAGCAUC	ACUCCCCC
	258	CGAUGGGG	CUGAUGA	х	GAA	AGUGAUGC	GCAUCACUC	CCCCAUCG
	26 5	CACAGGCC	CUGAUGA	х	GAA	AUGGGGGA	UCCCCCAUC	GGCCUGUG
	282	UUGCCUGU	CUGAUGA	Х	GAA	AUCCCUCC	GGAGGGAUA	ACAGGCAA
	292	UGCUGCAG	CUGAUGA	Х	GAA	AUUGCCUG	CAGGCAAUU	CUGCAGCA
10	29 3	GUGCUGCA	CUGAUGA	X	GAA	AAUUGCCU	AGGCAAUUC	UGCAGCAC
	304	CCAAGGUC	CUGAUGA	Х	GAA	AGGUGCUG	CAGCACCUU	GACCUUGG
	310	CCGUGUCC	CUGAUGA	х	GAA	AGGUCAAG	CUUGACCUU	GGACACGG
	341	CAGGUGUA	CUGAUGA	x	GAA	AGGCCCGU	ACGGGCCUC	UACACCUG
	343	UACAGGUG	CUGAUGA	Х	GAA	AGAGGCCC	GGGCCUCUA	CACCUGUA
15	351	GAGGUAUC	CUGAUGA	Х	GAA	ACAGGUGU	ACACCUGUA	GAUACCUC
	355	UAGGGAGG	CUGAUGA	Х	GAA	AUCUACAG	CUGUAGAUA	CCUCCCUA
	359	GAUGUAGG	CUGAUGA	х	GAA	AGGUAUCU	AGAUACCUC	CCUACAUC
	363	AGUAGAUG	CUGAUGA	Х	GAA	AGGGAGGU	ACCUCCCUA	CAUCUACU
	367	UCGAAGUA	CUGAUGA	х	GAA	AUGUAGGG	CCCUACAUC	UACUUCGA
20	36 9	CUUCGAAG	CUGAUGA	X	GAA	AGAUGUAG	CUACAUCUA	CUUCGAAG
	372	UUUCUUCG	CUGAUGA	X	GAA	AGUAGAUG	CAUCUACUU	CGAAGAAA
	373	uuuucuuc	CUGAUGA	Х	GAA	AAGUAGAU	AUCUACUUC	GAAGAAAA
	394	AGAUUGAA	CUGAUGA	х	GAA	AUUCCGCU	AGCGGAAUC	UUCAAUCU
	396	GUAGAUUG	CUGAUGA	Х	GAA	AGAUUCCG	CGGAAUCUU	CAAUCUAC
25	397	UGUAGAUU	CUGAUGA	X	GAA	AAGAUUCC	GGAAUCUUC	AAUCUACA
	401	AAUAUGUA	CUGAUGA	Х	GAA	AUUGAAGA	UCUUCAAUC	UACAUAUU
	403	CAAAUAUG	CUGAUGA	Х	GAA	AGAUUGAA	UUCAAUCUA	CAUAUUUG
	407	CUAACAAA	CUGAUGA	Х	GAA	AUGUAGAU	AUCUACAUA	UUUGUUAG
	409	CACUAACA	CUGAUGA	Х	GAA	AUAUGUAG	CUACAUAUU	UGUUAGUG
30	410	UCACUAAC	CUGAUGA	Х	GAA	AAUAUGUA	UACAUAUUU	GUUAGUGA
	413	GCAUCACU	CUGAUGA	Х	GAA	ACAAAUAU	AUAUUUGUU	AGUGAUGC
	414	UGCAUCAC	CUGAUGA	Х	GAA	AACAAAUA	UAUUUGUUA	GUGAUGCA
	429	UAUGAA AG	CUGAUGA	X	GAA	ACUCCCUG	CAGGGAGUC	CUUUCAUA

	432	CUCUAUGA CUGAUGA X GAA AGGACUCC	GGAGUCCUU UCAUAGAG
	433	UCUCUAUG CUGAUGA X GAA AAGGACUC	GAGUCCUUU CAUAGAGA
	434	AUCUCUAU CUGAUGA X GAA AAAGGACU	AGUCCUUUC AUAGAGAU
	437	UGCAUCUC CUGAUGA X GAA AUGAAAGG	CCUUUCAUA GAGAUGCA
5	45 5	AGUUUGGG CUGAUGA X GAA AUGUCAGU	ACUGACAUA CCCAAACU
	464	AUGUGCAC CUGAUGA X GAA AGUUUGGG	CCCAAACUU GUGCACAU
	491	GGGAUGAU CUGAUGA X GAA AGCUGUCU	AGACAGCUC AUCAUCCC
	494	CAGGGGAU CUGAUGA X GAA AUGAGCUG	CAGCUCAUC AUCCCCUG
	497	CGGCAGGG CUGAUGA X GAA AUGAUGAG	CUCAUCAUC CCCUGCCG
10	514	CGUUGGGU CUGAUGA X GAA ACGUCACC	GGUGACGUC ACCCAACG
	524	GUGACUGU CUGAUGA X GAA ACGUUGGG	CCCAACGUC ACAGUCAC
•	530	UUUAGGGU CUGAUGA X GAA ACUGUGAC	GUCACAGUC ACCCUAAA
	536	AACUUUUU CUGAUGA X GAA AGGGUGAC	GUCACCCUA AAAAAGUU
	544	CAAAUGGA CUGAUGA X GAA ACUUUUUU	AAAAAAGUU UCCAUUUG
15	54 5	UCAAAUGG CUGAUGA X GAA AACUUUUU	AAAAAGUUU CCAUUUGA
	54 6	AUCAAAUG CUGAUGA X GAA AAACUUUU	AAAAGUUUC CAUUUGAU
	550	GAGUAUCA CUGAUGA X GAA AUGGAAAC	GUUUCCAUU UGAUACUC
	551	AGAGUAUC CUGAUGA X GAA AAUGGAAA	UUUCCAUUU GAUACUCU
	55 5	GGUAAGAG CUGAUGA X GAA AUCAAAUG	CAUUUGAUA CUCUUACC
20	558	AGGGGUAA CUGAUGA X GAA AGUAUCAA	UUGAUACUC UUACCCCU
	560	UCAGGGGU CUGAUGA X GAA AGAGUAUC	GAUACUCUU ACCCCUGA
	561	AUCAGGGG CUGAUGA X GAA AAGAGUAU	AUACUCUUA CCCCUGAU
	581	UCCCAUGU CUGAUGA X GAA AUUCUUUG	CAAAGAAUA ACAUGGGA
	594	GCCUCUCC CUGAUGA X GAA ACUGUCCC	GGGACAGUA GGAGAGGC
25	604	CUAUUAUA CUGAUGA X GAA AGCCUCUC	GAGAGGCUU UAUAAUAG
	605	GCUAUUAU CUGAUGA X GAA AAGCCUCU	AGAGGCUUU AUAAUAGC
	606	UGCUAUUA CUGAUGA X GAA AAAGCCUC	GAGGCUUUA UAAUAGCA
	608	UUUGCUAU CUGAUGA X GAA AUAAAGCC	GGCUUUAUA AUAGCAAA
	611	GCAUUUGC CUGAUGA X GAA AUUAUAAA	UUUAUAAUA GCAAAUGC
30	625	UCUCUUUG CUGAUGA X GAA ACGUUGCA	UGCAACGUA CAAAGAGA
	635	AGCAGUCC CUGAUGA X GAA AUCUCUUU	AAAGAGAUA GGACUGCU
	662	UGCCCGUU CUGAUGA X GAA ACGGUGGC	GCCACCGUC AACGGGCA
	676	UUGUCUGG CUGAUGA X GAA ACAGGUGC	GCACCUGUA CCAGACAA

	688	GGGUCAGA	CUGAUGA	X	GAA	AGUUUGUC	GACAAACUA	UCUGACCC
	690	AUGGGUCA	CUGAUGA	х	GAA	AUAGUUUG	CAAACUAUC	UGACCCAU
	699	GGUCUGCC	CUGAUGA	X	GAA	AUGGGUCA	UGACCCAUC	GGCAGACC
	711	UAGGAUUG	CUGAUGA	X	GAA	AUUGGUCU	AGACCAAUA	CAAUCCUA
5	716	ACAUCUAG	CUGAUGA	X	GAA	AUUGUAUU	AAUACAAUC	CUAGAUGU
	719	UGGACAUC	CUGAUGA	Х	GAA	AGGAUUGU	ACAAUCCUA	GAUGUCCA
	725	CGUAUUUG	CUGAUGA	Х	GAA	ACAUCUAG	CUAGAUGUC	CAAAUACG
	731	GGCGGGCG	CUGAUGA	X	GAA	AUUUGGAC	GUCCAAAUA	CGCCCGCC
	758	UGCCCGUG	CUGAUGA	Х	GAA	AGCAGUCU	AGACUGCUC	CACGGGCA
10	771	GAGGACAA	CUGAUGA	Х	GAA	AGUCUGCC	GGCAGACUC	UUGUCCUC
	773	UUGAGGAC	CUGAUGA	X	GAA	AGAGUCUG	CAGACUCUU	GUCCUCAA
	776	CAGUUGAG	CUGAUGA	Х	GAA	ACAAGAGU	ACUCUUGUC	CUCAACUG
	77 9	GUGCAGUU	CUGAUGA	х	GAA	AGGACAAG	CUUGUCCUC	AACUGCAC
	803	CUCGUAUU	CUGAUGA	х	GAA	AGCUCCGU	ACGGAGCUC	AAUACGAG
15	807	CACCCUCG	CUGAUGA	Х	GAA	AUUGAGCU	AGCUCAAUA	CGAGGGUG
	831	ACCAGGGU	CUGAUGA	Х	GAA	AUUCCAGC	GCUGGAAUU	ACCCUGGU
	832	UACCAGGG	CUGAUGA	X	GAA	AAUUCCAG	CUGGAAUUA	CCCUGGUA
	840	AGUUGCUU	CUGAUGA	X	GAA	ACCAGGGU	ACCCUGGUA	AAGCAACU
	84 9	UGCUCUCU	CUGAUGA	Х	GAA	AGUUGCUU	AAGCAACUA	AGAGAGCA
20	85 9	GCCUUAUA	CUGAUGA	Х	GAA	AUGCUCUC	GAGAGCAUC	UAUAAGGC
	861	CUGCCUUA	CUGAUGA	X	GAA	AGAUGCUC	GAGCAUCUA	UAAGGCAG
	863	CGCUGCCU	CUGAUGA	X	GAA	AUAGAUGC	GCAUCUAUA	AGGCAGCG
	87 5	CUCCGGUC	CUGAUGA	X	GAA	AUCCGCUG	CAGCGGAUU	GACCGGAG
	888	GUUGUGGG	CUGAUGA	X	GAA	AUGGCUCC	GGAGCCAUU	CCCACAAC
25	889	UGUUGUGG	CUGAUGA	X	GAA	AAUGGCUC	GAGCCAUUC	CCACAACA
	904	CACUGUGG	CUGAUGA	Х	GAA	ACACAUUG	CAAUGUGUU	CCACAGUG
	905	ACACUGUG	CUGAUGA	X	GAA	AACACAUU	AAUGUGUUC	CACAGUGU
	914	AUCUUAAG	CUGAUGA	X	GAA	ACACUGUG	CACAGUGUU	CUUAAGAU
	91 5	GAUCUUAA	CUGAUGA	Х	GAA	AACACUGU	ACAGUGUUC	UUAAGAUC
30	917	UUGAUCUU	CUGAUGA	X	GAA	AGAACACU	AGUGUUCUU	AAGAUCAA
	918	GUUGAUCU	CUGAUGA	X	GAA	AAGAACAC	GUGUUCUUA	AGAUCAAC
	923	ACAUUGUU	CUGAUGA	X	GAA	AUCUUAAG	CUUAAGAUC	AACAAUGU
	953	CAGGUGUA	CUGAUGA	X	GAA	AGCCCCUU	AAGGGCUC	UACACCUG

	955	GACAGGUG	CUGAUGA	2	GA/	A AGAGCCCC	GGGGCUCUA CACCUGUC
	96 3	CUUCACGO	CUGAUGA	.)	GA/	A ACAGGUGU	ACACCUGUC GCGUGAAG
	97 9	GGAACGAG	CUGAUGA	. >	GA	ACCCACUC	GAGUGGGUC CUCGUUCC
	982	ACUGGAAC	CUGAUGA	. >	GAZ	AGGACCCA	UGGGUCCUC GUUCCAGU
5	98 5	AAGACUGG	CUGAUGA	. }	GAA	ACGAGGAC	GUCCUCGUU CCAGUCUU
	986	AAAGACUG	CUGAUGA	. >	GAA	AACGAGGA	UCCUCGUUC CAGUCUUU
	991	UGUUGAAA	CUGAUGA	. X	GAA	ACUGGAAC	GUUCCAGUC UUUCAACA
	993	GGUGUUGA	CUGAUGA	. X	GAA	AGACUGGA	UCCAGUCUU UCAACACC
	994	AGGUGUUG	CUGAUGA	X	GAA	AAGACUGG	CCAGUCUUU CAACACCU
10	995	GAGGUGUU	CUGAUGA	Х	GAA	AAAGACUG	CAGUCUUUC AACACCUC
	1003	CAUGCACG	CUGAUGA	X	GAA	AGGUGUUG	CAACACCUC CGUGCAUG
	1015	CUUUUUCA	CUGAUGA	Х	GAA	ACACAUGC	GCAUGUGUA UGAAAAAG
	1027	CACUGAUG	CUGAUGA	Х	GAA	AUCCUUUU	AAAAGGAUU CAUCAGUG
	1028	ACACUGAU	CUGAUGA	Х	GAA	AAUCCUUU	AAAGGAUUC AUCAGUGU
15	1031	UUCACACU	CUGAUGA	X	GAA	AUGAAUCC	GGAUUCAUC AGUGUGAA
	1044	CUGCUUCC	CUGAUGA	X	GAA	AUGUUUCA	UGAAACAUC GGAAGCAG
	1084	GCCGAUAG	CUGAUGA	X	GAA	ACCGUCUU	AAGACGGUC CUAUCGGC
	1087	ACAGCCGA	CUGAUGA	X	GAA	AGGACCGU	ACGGUCCUA UCGGCUGU
	1089	GGACAGCC	CUGAUGA	X	GAA	AUAGGACC	GGUCCUAUC GGCUGUCC
20	1096	CUUUCAUG	CUGAUGA	X	GAA	ACAGCCGA	UCGGCUGUC CAUGAAAG
	1114	GGGAGGGG	CUGAUGA	X	GAA	AGGCCUUC	GAAGGCCUU CCCCUCCC
	1115	GGGGAGGG	CUGAUGA	X	GAA	AAGGCCUU	AAGGCCUUC CCCUCCCC
	1120	UUUCUGGG	CUGAUGA	Х	GAA	AGGGGAAG	CUUCCCCUC CCCAGAAA
	1130	AACCAUAC	CUGAUGA	X	GAA	AUUUCUGG	CCAGAAAUC GUAUGGUU
25	1133	UUUAACCA	CUGAUGA	Х	GAA	ACGAUUUC	GAAAUCGUA UGGUUAAA
	1138	CAUCUUUU	CUGAUGA	X	GAA	ACCAUACG	CGUAUGGUU AAAAGAUG
	1139	CCAUCUUU	CUGAUGA	Х	GAA	AACCAUAC	GUAUGGUUA AAAGAUGG
	1150	UUGCAGGC	CUGAUGA	X	GAA	AGCCAUCU	AGAUGGCUC GCCUGCAA
	1162	CAGACUUC	CUGAUGA	X	GAA	AUGUUGCA	UGCAACAUU GAAGUCUG
30	1168	AGCGAGCA	CUGAUGA	X	GAA	ACUUCAAU	AUUGAAGUC UGCUCGCU
	1173	CAAAUAGC	CUGAUGA	X	GAA	AGCAGACU	AGUCUGCUC GCUAUUUG
	1177	GUACCAAA	CUGAUGA	X	GAA	AGCGAGCA	UGCUCGCUA UUUGGUAC
	1179	AUGUACCA	CUGAUGA	Х	GAA	AUAGCGAG	CUCGCUAUU UGGUACAU

	1180	CAUGUACC	CUGAUGA	Х	GAA	AAUAGCGA	UCGCUAUUU	GGUACAUG
	1184	UAGCCAUG	CUGAUGA	X	GAA	ACCAAAUA	UAUUUGGUA	CAUGGCUA
	1192	UUAAUGAG	CUGAUGA	Х	GAA	AGCC AU GU	ACAUGGCUA	CUCAUUAA
	1195	UAAUUAAU	CUGAUGA	X	GAA	AGUAGCCA	UGGCUACUC	AUUAAUUA
5	1198	UGAUAAUU	CUGAUGA	X	GAA	AUGAGUAG	CUACUCAUU	AAUUAUCA
	1199	UUGAUAAU	CUGAUGA	X	GAA	AAUGAGUA	UACUCAUUA	AUUAUCAA
	1202	UCUUUGAU	CUGAUGA	X	GAA	AUUAAUGA	UCAUUAAUU	AUCAAAGA
	1203	AUCUUUGA	CUGAUGA	Х	GAA	AAUUAAUG	CAUUAAUUA	UCAAAGAU
	1205	ACAUCUUU	CUGAUGA	Х	GAA	AUAAUUAA	UUAAUUAUC	AAAGAUGU
10	1237	AGAUCGUA	CUGAUGA	x	GAA	AGUCCCCU	AGGGGACUA	UACGAUCU
	1239	CAAGAUCG	CUGAUGA	Х	GAA	AUAGUCCC	GGGACUAUA	CGAUCUUG
	1244	CCCAGCAA	CUGAUGA	x	GAA	AUCGUAUA	UAUACGAUC	UUGCUGGG
	1246	UGCCCAGC	CUGAUGA	Х	GAA	AGAUCGUA	UACGAUCUU	GCUGGGCA
	1256	GACUGCUU	CUGAUGA	Х	GAA	AUGCCCAG	CUGGGCAUA	AAGCAGUC
15	1264	AUAGCCUU	CUGAUGA	X	GAA	ACUGCUUU	AAAGCAGUC	AAGGCUAU
	1271	AAAUUUUU	CUGAUGA	Х	GAA	AGCCUUGA	UCAAGGCUA	UUUAAAAA
	127 3	GGUUUUUA	CUGAUGA	X	GAA	AUAGCCUU	AAGGCUAUU	UAAAAACC
	1274	AGGUUUUU	CUGAUGA	X	GAA	AAUAGCCU	AGGCUAUUU	AAAAACCU
	1275	GAGGUUUU	CUGAUGA	х	GAA	AAAUAGCC	GGCUAUUUA	AAAACCUC
20	1283	GUGGCAGU	CUGAUGA	X	GAA	AGGUUUUU	AAAAACCUC	ACUGCCAC
	1293	UACAAUGA	CUGAUGA	X	GAA	AGUGGCAG	CUGCCACUC	UCAUUGUA
	1295	UUUACAAU	CUGAUGA	X	GAA	AGAGUGGC	GCCACUCUC	AUUGUAAA
	1298	ACGUUUAC	CUGAUGA	X	GAA	AUGAGAGU	ACUCUCAUU	GUAAACGU
	1301	UUCACGUU	CUGAUGA	Х	GAA	ACAAUGAG	CUCAUUGUA	AACGUGAA
25	1314	GUAGAUCU	CUGAUGA	х	GAA	AGGUUUCA	UGAAACCUC	AGAUCUAC
	1319	UUUUCGUA	CUGAUGA	Х	GAA	AUCUGAGG	CCUCAGAUC	UACGAAAA
	1321	ACUUUUCG	CUGAUGA	X	GAA	AGAUCUGA	UCAGAUCUA	CGAAAAGU
	1330	AGGACACG	CUGAUGA	Х	GAA	ACUUUUCG	CGAAAAGUC	CGUGUCCU
	1336	GAAGCGAG	CUGAUGA	Х	GAA	ACACGGAC	GUCCGUGUC	CUCGCUUC
30	1339	UUGGAAGC	CUGAUGA	Х	GAA	AGGACACG	CGUGUCCUC	GCUUCCAA
	1343	GGGCUUGG	CUGAUGA	X	GAA	AGCGAGGA	UCCUCGCUU	CCAAGCCC
	1344	UGGGCUUG	CUGAUGA	X	GAA	AAGCGAGG	CCUCGCUUC	CAAGCCCA
	1356	CGGAUAGA	CUGAUGA	Х	GAA	AGGUGGGC	GCCCACCUC	UCUAUCCG

, s.

	1358	AGCGGAUA CUGAUGA X GAA AGAG	GUGG CCACCUCUC UAUCCGCU
	1360	CCAGCGGA CUGAUGA X GAA AGAG	AGGU ACCUCUCUA UCCGCUGG
	1362	GCCCAGCG CUGAUGA X GAA AUAG	AGAG CUCUCUAUC CGCUGGGC
	1382	CAAGUGAG CUGAUGA X GAA ACUU	GUCU AGACAAGUC CUCACUUG
5	1385	GUGCAAGU CUGAUGA X GAA AGGA	CUUG CAAGUCCUC ACUUGCAC
	1389	CACGGUGC CUGAUGA X GAA AGUGA	AGGA UCCUCACUU GCACCGUG
	1399	GGAUGCCA CUGAUGA X GAA ACACO	GGUG CACCGUGUA UGGCAUCC
	1406	GGCCGAGG CUGAUGA X GAA AUGCC	CAUA UAUGGCAUC CCUCGGCC
	1410	UGUUGGCC CUGAUGA X GAA AGGGA	UGC GCAUCCCUC GGCCAACA
10	1421	AGCCACGU CUGAUGA X GAA AUUGU	TUGG CCAACAAUC ACGUGGCU
	1430	GGGUGCCA CUGAUGA X GAA AGCCA	ACGUGGCUC UGGCACCC
	1443	AUUGUGGU CUGAUGA X GAA ACAGG	GGU ACCCCUGUC ACCACAAU
	. 1452	UUUGGAGU CUGAUGA X GAA AUUGU	GGU ACCACAAUC ACUCCAAA
	1456	UUUCUUUG CUGAUGA X GAA AGUGA	UUG CAAUCACUC CAAAGAAA
15	1468	AGAAGUCA CUGAUGA X GAA ACCUU	UCU AGAAAGGUA UGACUUCU
	1474	CAGUGCAG CUGAUGA X GAA AGUCA	UAC GUAUGACUU CUGCACUG
	1475	UCAGUGCA CUGAUGA X GAA AAGUC	AUA UAUGACUUC UGCACUGA
	1495	GGAUAAAG CUGAUGA X GAA AUUCU	UCA UGAAGAAUC CUUUAUCC
	1498	CCAGGAUA CUGAUGA X GAA AGGAU	UCU AGAAUCCUU UAUCCUGG
20	1499	UCCAGGAU CUGAUGA X GAA AAGGA	JUC GAAUCCUUU AUCCUGGA
	1500	AUCCAGGA CUGAUGA X GAA AAAGG	AUU AAUCCUUUA UCCUGGAU
	1502	GGAUCCAG CUGAUGA X GAA AUAAA	GGA UCCUUUAUC CUGGAUCC
	1509	GCUGCUGG CUGAUGA X GAA AUCCAG	GGA UCCUGGAUC CCAGCAGC
	1522	UGUUUCCU CUGAUGA X GAA AGUUGO	CUG CAGCAACUU AGGAAACA
25	1523	CUGUUUCC CUGAUGA X GAA AAGUUC	GCU AGCAACUUA GGAAACAG
	15 35	AUGCUCUC CUGAUGA X GAA AUUCUC	GUU AACAGAAUU GAGAGCAU
	1544	CGCUGAGA CUGAUGA X GAA AUGCUC	CUC GAGAGCAUC UCUCAGCG
	1546	UGCGCUGA CUGAUGA X GAA AGAUGO	CUC GAGCAUCUC UCAGCGCA
	1548	CAUGCGCU CUGAUGA X GAA AGAGAU	GC GCAUCUCUC AGCGCAUG
30	1562	CCUUCUAU CUGAUGA X GAA ACCGUC	AUGACGGUC AUAGAAGG
	1565	GUUCCUUC CUGAUGA X GAA AUGACO	GU ACGGUCAUA GAAGGAAC
	1578	AACCGUCU CUGAUGA X GAA AUUUGU	UC GAACAAAUA AGACGGUU
	1586	AAUGUGCU CUGAUGA X GAA ACCGUC	UU AAGACGGIII AGCACAIII

	1587	CAAUGUGC	CUGAUGA	Х	GAA	AACCGUCU	AGACGGUUA	GCACAUUG
	1594	CCACCACC	CUGAUGA	Х	GAA	AUGUGCUA	UAGCACAUU	GGUGGUGG
	1609	GGGUCUGA	CUGAUGA	X	GAA	AGUCAGCC	GGCUGACUC	UCAGACCC
	1611	AGGGGUCU	CUGAUGA	Х	GAA	AGAGUCAG	CUGACUCUC	AGACCCCU
5	1625	CAGCUGUA	CUGAUGA	х	GAA	AUUCCAGG	CCUGGAAUC	UACAGCUG
	1627	GGCAGCUG	CUGAUGA	X	GAA	AGAUUCCA	UGGAAUCUA	CAGCUGCC
	1642	UUUUAUUG	CUGAUGA	Х	GAA	AGGCCCGG	CCGGGCCUU	CAAUAAAA
	1643	AUUUUAUU	CUGAUGA	X	GAA	AAGGCCCG	CGGGCCUUC	AAUAAAu
	1647	CCCUAUUU	CUGAUGA	Х	GAA	AUUGAAGG	CCUUCAAUA	AAAUAGGG
10	1652	ACAGUCCC	CUGAUGA	Х	GAA	UUAUUUA	AAUAAAAUA	GGGACUGU
	1673	UUUAAAAUU	CUGAUGA	Х	GAA	AUGUUUCU	AGAAACAUA	AAAUUUUA
	1678	UGACAUAA	CUGAUGA	Х	GAA	AUUUUAUG	CAUAAAAUU	UUAUGUCA
	1679	GUGACAUA	CUGAUGA	X	GAA	UAUUUUAA	AUAAAAUUU	UAUGUCAC
	1680	UGUGACAU	CUGAUGA	X	GAA	AUUUUAAA	UUUUAAAAU	AUGUCACA
15	1681	CUGUGACA	CUGAUGA	Х	GAA	UUUUAAAA	AAAAUUUUA	UGUCACAG
	1685	ACAUCUGU	CUGAUGA	Х	GAA	ACAUAAAA	UUUUAUGUC	ACAGAUGU
	1705	AAACGUGA	CUGAUGA	X	GAA	AGCCAUUC	GAAUGGCUU	UCACGUUU
	1706	GAAACGUG	CUGAUGA	X	GAA	AAGCCAUU	AAUGGCUUU	CACGUUUC
	1707	GGAAACGU	CUGAUGA	Х	GAA	AAAGCCAU	AUGGCUUUC	ACGUUUCC
20	1712	UCCAAGGA	CUGAUGA	X	GAA	ACGUGAAA	UUUCACGUU	UCCUUGGA
	1713	UUCCAAGG	CUGAUGA	X	GAA	AACGUGAA	UUCACGUUU	CCUUGGAA
	1714	UUUCCAAG	CUGAUGA	Х	GAA	AAACGUGA	UCACGUUUC	CUUGGAAA
	1717	ncnnnncc	CUGAUGA	X	GAA	AGGAAACG	CGUUUCCUU	GGAAAAGA
	1756	CCACACAG	CUGAUGA	Χ	GAA	ACAGUUUC	GAAACUGUC	CUGUGUGG
25	1766	AAUUUAUU	CUGAUGA	х	GAA	ACCACACA	UGUGUGGUC	UUAAAUAA
	1770	CAGGAAUU	CUGAUGA	Х	GAA	AUUGACCA	UGGUCAAUA	AAUUCCUG
	1774	UGUACAGG	CUGAUGA	Х	GAA	AUUUAUUG	CAAUAAAUU	CCUGUACA
	1775	CUGUACAG	CUGAUGA	X	GAA	UUAUUUAA	AAUAAAUUC	CUGUACAG
	1780	UGUCUCUG	CUGAUGA	Х	GAA	ACAGGAAU	AUUCCUGUA	CAGAGACA
30	1790	AUCCAGGU	CUGAUGA	X	GAA	AUGUCUCU	AGAGACAUU	ACCUGGAU
	1791	AAUCCAGG	CUGAUGA	X	GAA	AAUGUCUC	GAGACAUUA	CCUGGAUU
	1799	CGUAGCAG	CUGAUGA	X	GAA	AUCCAGGU	ACCUGGAUU	CUGCUACG
	1800	CCGUAGCA	CUGAUGA	Х	GAA	AAUCCAGG	CCUGGAUUC	UGCUACGG

	1805	ACUGUCCG CUGAUGA X GAA AGCAGAAU	AUUCUGCUA CGGACAGU
	1814	CUGUUGUU CUGAUGA X GAA ACUGUCCG	CGGACAGUU AACAACAG
	1815	UCUGUUGU CUGAUGA X GAA AACUGUCC	GGACAGUUA ACAACAGA
	1836	GCUGAUAC CUGAUGA X GAA AUGGUGCA	UGCACCAUA GUAUCAGC
5	1839	CUUGCUGA CUGAUGA X GAA ACUAUGGU	ACCAUAGUA UCAGCAAG
	1841	UGCUUGCU CUGAUGA X GAA AUACUAUG	CAUAGUAUC AGCAAGCA
	1866	GUAAUCUU CUGAUGA X GAA AGUGGUGG	CCACCACUC AAGAUUAC
	1872	GAUGGAGU CUGAUGA X GAA AUCUUGAG	CUCAAGAUU ACUCCAUC
	1873	UGAUGGAG CUGAUGA X GAA AAUCUUGA	UCAAGAUUA CUCCAUCA
10	1876	GAGUGAUG CUGAUGA X GAA AGUAAUCU	AGAUUACUC CAUCACUC
	1880	UUCAGAGU CUGAUGA X GAA AUGGAGUA	UACUCCAUC ACUCUGAA
	1884	AAGGUUCA CUGAUGA X GAA AGUGAUGG	CCAUCACUC UGAACCUU
	1892	UUGAUGAC CUGAUGA X GAA AGGUUCAG	CUGAACCUU GUCAUCAA
	1895	UUCUUGAU CUGAUGA X GAA ACAAGGUU	AACCUUGUC AUCAAGAA
15	1898	ACGUUCUU CUGAUGA X GAA AUGACAAG	CUUGUCAUC AAGAACGU
	1909	CUUCUAGA CUGAUGA X GAA ACACGUUC	GAACGUGUC UCUAGAAG
	1911	GUCUUCUA CUGAUGA X GAA AGACACGU	ACGUGUCUC UAGAAGAC
	191 3	GAGUCUUC CUGAUGA X GAA AGAGACAC	GUGUCUCUA GAAGACUC
	1921	AGGUGCCC CUGAUGA X GAA AGUCUUCU	AGAAGACUC GGGCACCU
20	1930	UGCACGCA CUGAUGA X GAA AGGUGCCC	GGGCACCUA UGCGUGCA
	1952	CCUGUGUA CUGAUGA X GAA AUGUUCCU	AGGAACAUA UACACAGG
	1954	CCCCUGUG CUGAUGA X GAA AUAUGUUC	GAACAUAUA CACAGGGG
	1970	UUCCGAAG CUGAUGA X GAA AUGUCUUC	GAAGACAUC CUUCGGAA
	1973	GUCUUCCG CUGAUGA X GAA AGGAUGUC	GACAUCCUU CGGAAGAC
25	1974	UGUCUUCC CUGAUGA X GAA AAGGAUGU	ACAUCCUUC GGAAGACA
	1988	CUAACGAG CUGAUGA X GAA ACUUCUGU	ACAGAAGUU CUCGUUAG
	1 98 9	UCUAACGA CUGAUGA X GAA AACUUCUG	CAGAAGUUC UCGUUAGA
	1991	UCUCUAAC CUGAUGA X GAA AGAACUUC	GAAGUUCUC GUUAGAGA
	1994	GAAUCUCU CUGAUGA X GAA ACGAGAAC	GUUCUCGUU AGAGAUUC
30	1995	CGAAUCUC CUGAUGA X GAA AACGAGAA	UUCUCGUUA GAGAUUCG
	2001	CGCUUCCG CUGAUGA X GAA AUCUCUAA	UUAGAGAUU CGGAAGCG
	2002	GCGCUUCC CUGAUGA X GAA AAUCUCUA	UAGAGAUUC GGAAGCGC
	2021	AGGUUUUG CUGAUGA X GAA AGCAGGUG	CACCUGCUU CAAAACCU

PCT/US96/17480

2038 AGACCUCG CUGAUGA X GAA AGUCACUG CAGUGACUA CUGAUGA CUGAUGA X GAA ACCUCGUA UACGAGGUC CO CAGUGAUGA X GAA AGCUCGUA COGAGGUCUC CO CACUGAUGA CUGAUGA X GAA AGCCUCG CGAGGUCUC COGAGGUCUC COGAGGUCUC COGAGGUCUC COGAGGUCUC COGAGGUCUC COGAGGUCUC COGAGGUCUC CUGAUGA X GAA AGCCACUG CAGUGGCUCUA COGAGGUCUC COGAGGUCUC COGAGGUCUC COGAUGA X GAA AGGCCACUG CAGUGGCUCUA COGAGGUCUC CUGAUGA X GAA AGGCCACUG GUGGCUCUA COGAGGUCUC CUGAUGA X GAA AGGUCGUA UACGACCUUA GACACCUUA GACACCUUA GACACCUUA GACACCUUA COGAGGUCUA COGAGGUCUA COGAGGUCUA COGAGGUCUA COGAGGUCUA COGAGGUCUA COGAGGUCUA COGAGGUCUA COGACGUCUA COGAGGUCUA COGAGCCUUA GACACCUUA GACACCUUA GACACCUUA GACACCUUA GACACCUUA GACACCUUA COGAGGUCUA COGAGCCUUA COGAGGUCUA COGAGGUCUA COGAGCCUUA GACACCUUA GACACACACUA COGAGGUCUA COGAGGA X GAA ACCCACUCU AGAGGUCUA COCACACACACUA COGAUGA X GAA ACCCACGU CCCCCCCCCCUCA COGAGCAUA X GAA ACCCACGUA COCACACACACUA COGAGUACA X GAA ACCCACGU CCCCCCCCCUCA COGAGACUA COGAUGA X GAA ACCCACGU CCCCGGGAAUUA COCACACACACACUA COCACACACACACACACACACACACACACACACACACA	ACCUGCUUC AAAACCUC
2045 CUGAUGGA CUGAUGA X GAA ACCUCGUA UACGAGGUC UCACUGUA CACUGAUGA CUGAUGA X GAA AGACCUCG CGAGGUCUC CACUGAUGA CUGAUGA X GAA AGACCUCG CGAGGUCUC CACUGAUGA CUGAUGA X GAA AGACCAUG CAGUGGCUCU ACCUGAUGA X GAA AGGUCGUA UACGACCUU ACCUGAUGA X GAA AGGUCGUA UACGACCUU ACCUGAUGA X GAA AGGUCGUA UACGACCUU ACCUGAUGA X GAA AGGUCGUA UAGACCUCU ACCUGAUGA X GAA ACAGUCUA UAGACCUCU ACCUGAUGA X GAA ACCUCUU AGACCUUA ACCUCU ACCUGAUGA X GAA ACCUCUU AGACCUCU AGACCUUA ACCUCU AGACCUUA ACCUCU AGACCUUA ACCUCU ACCUCUCU ACCUCU ACCUCUAGA X GAA ACCUCUCU ACCUCUAGA X GAA ACCUAGU ACCUCUCU ACCUCUAGA X GAA ACCUAGU ACCUCUGUU ACCUCUAGA X GAA ACCUAGU ACCUCUGUU ACCUCUAGA X GAA ACCAAGU ACCUUGGUU ACCUCUAGA X GAA ACCAAGU ACCUUGGUU ACCUCUAGA X GAA ACCAAGU ACCUCGG CCGGGAAUUA ACCUCUAGA X GAA AUAUCCCG CCGGGAAUUA ACCUCUAGA X GAA AUAUCCCG CCGGGAAUUA ACCUCUAGA X GAA AUAUCCCG CCGGGAAUUA ACCUCUAGA X GAA AUAAUCCC GCGGGAAUUA ACCUCUAGA X GAA AAAAAAAUAU AAUAUUUUA ACCUCUAGA X GAA AAAAAAAUAU AAUAAUUUUA ACCUCUAGA X GAA AAAAAAAUAU AAUAAUUUUA ACCUCUAGA X GAA AAAAAAAUAUU AAUAAUUUUA ACCUCUAGA X GAA AAAAAAAUAAU AAUAAUUUUA ACCUCAAAAA CUGAUGA X GAA AAAAAAAAUAAU AAUAAUUUUA ACCUCUAGA X GAA AAAAAAAAAAAAAAAAAAAAAAAAAAAAA	CAAAACCUC AGUGACUA
5 2047 CACUGAUG CUGAUGA X GAA AGACCUCG CGAGGUCUC CACAGAAUUA CUGAUGA X GAA AGCCACUG CACGGGAGUCUC CACAGGGCACU CUGAUGA X GAA AGCCACUG CAGUGGCCUC CACAGGCACUG CUGAUGA X GAA AGCCACUG CAGUGGCCUC CACAGGCCAC CUGAUGA X GAA AGCCACUG CAGUGGCUCU CUGAUGA X GAA AGGUCGUA UACGACCUU AGCACGCAC GUGACCACUG CUGAUGA X GAA AGGUCGUA UACGACCUU AGCACCUUA GAAAAAAUAAU AUUAUUUUUA GAACACCUC CUGAUGA X GAA AACAGCAC CCCGGGAAUU ACGACCUU AGAACAGCAC CUGAUGA X GAA ACACGCAC CCCCAGAACAACAC CUGAUGA X GAA ACACCUCU AGAGCACCUC CUGAUGA X GAA ACCACAGCAC CCCCAGAACAACAC CUGAUGA X GAA ACCACAGCAC CCCCAGACCAC CUGAUGA X GAA ACCACCUCU AGAGCACCUC AGACCACACACACACACACACACACACACACACACACA	CAGUGACUA CGAGGUCU
2051 GAGCCACU CUGAUGA X GAA AUGGAGAC GUCUCCAUC AC 2059 AGGUCGUA CUGAUGA X GAA AGCCACUG CAGUGGCUCU DA 2061 UAAGGUCG CUGAUGA X GAA AGGCCACUG CAGUGGCUCU AC 2068 GACAGUCU CUGAUGA X GAA AGGUCGUA UACGACCUU AC 2068 GACAGUCU CUGAUGA X GAA AGGUCGUA UACGACCUU AC 2076 UCUAGCUU CUGAUGA X GAA AAGGUCGU UAGACCUUU AC 2076 UCUAGCUU CUGAUGA X GAA ACAGUCUA UAGACUGUC AA 2090 GGCGCGGG CUGAUGA X GAA ACACUCU AGAGGUGUC AC 2090 GGCGCGGG CUGAUGA X GAA ACACUCU AGAGGUGUC CUGAUGA X GAA ACCACUCU AGAGGUGUC CUGAUGA X GAA ACCACUCU AGAGCUUA AGAGGUGUC CUGAUGA X GAA ACCAAGUC CUGAUGA X GAA ACCAAGUC CUGAUGA X GAA ACCAAGUC CACUUGGUU CA 2113 UGUUUUUG CUGAUGA X GAA ACCAAGUC CACUUGGUU CA 2114 UUGUUUUU CUGAUGA X GAA ACCAAGU ACUUGGUUC AA 2114 UUGUUUUU CUGAUGA X GAA ACCAAGU ACUUGGUUC AA 2112 UCUUGUUG CUGAUGA X GAA AUUUUGUG CACAAAAUA CA 2132 UCUUGUUG CUGAUGA X GAA AUUUUGUG CACAAAAUA CA 2132 UCUUGUUG CUGAUGA X GAA AUUUCCGG CCGGGAAUUA CUGAUGA X GAA AUUCCCGG CCGGGAAUUA CUGAUGA X GAA AUUAUCCGG CGGGAAUUA UCUAUGUG CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2153 GGUCCUAA CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAAAAAUAAU AAUUAUUUU AGAUCACUU CUGAUGA X GAA AAAAAAAUA AUUAUUUUU AA 2156 CUGGUCCU CUGAUGA X GAA AAAAAAAAUA AUUAUUUU AA 2160 CUUUCAAU CUGAUGA X GAA AAAAAAAAA ACAGCGU CACGCUGUUU AU 2160 CUUUCAAU CUGAUGA X GAA AAAAAAAAA CAGCGU CACGCUGUUU AU 2160 CUUUCAAA CUGAUGA X GAA AAAAAAAAA CAGCGU ACGCUGUUU AU 2160 CUUUCAAA CUGAUGA X GAA AAAAAAAAA CAGCGU CACGCUGUUU AU 2160 CUGAUGA X GAA AAAAAAAAA CAGCGU CACGCUGUUU AU 2160 CUUUCAAA CUGAUGA X GAA AAAAAAAAAA CAGCGU CACGCUGUUU AA 2161 ACCUUUCAA CUGAUGA X GAA AAAAAAAAA CAGCG CACGCUGUUUA CUGAUGA X GAA AAAAAAAAAA CAGCGU CACGCUGUUUA AAAAAAA	UACGAGGUC UCCAUCAG
2059 AGGUCGUA CUGAUGA X GAA AGCCACUG CAGUGGCUC UA 2061 UAAGGUCG CUGAUGA X GAA AGCCACUG GUGGCUCUA CO 2068 GACAGUCU CUGAUGA X GAA AGGUCGUA UACGACCUU AG 2069 UGACAGUC CUGAUGA X GAA AAGGUCGU ACGACCUUA GA 2076 UCUAGCUU CUGAUGA X GAA ACAGUCUA UAGACCUUA GA 2082 GACACCUC CUGAUGA X GAA ACAGUCUA UAGACUGUC AA 2090 GGCGCGGG CUGAUGA X GAA ACACUCU AGAGGUGUC CUGAUGA X GAA ACACUCU AGAGGUGUC CUGAUGA X GAA ACCAUCU AGAGGUGUC CUGAUGA X GAA ACCACUCU AGAGGUGUC CUGAUGA X GAA ACCACUCU AGAGGUGUC CUGAUGA X GAA ACCACUCU AGAGGUGUC CUGAUGA X GAA ACCAAGUC CUCCAGAUC ACCACAGUC CUGAUGA X GAA ACCAAGUC AGAUCACUU GCAUGACCU AGAUCACUU GCAUGACCUU AGAUCACUU GCAUGACCU CUGAUGA X GAA ACCAAGUC CUCCAGAUC ACCACAGUC CUGAUGA X GAA ACCAAGUC CUCCAGAUC ACCACAGUC CUCAGAUC ACCACAGUC ACCACAGUC ACCACAGUC ACCACAGUC ACCACAAGUC ACCACAGUC ACCACAGUC ACCACAGUC ACCACAAGUC ACCACAGUC ACCACAAGUC ACCACAAAUA ACCACAGUC ACCACAGUCU ACCACACAGUC ACCACAGUCU ACCACACAGUC ACCACACAGUC ACCACCACCUC ACCACCUCUC ACCACCUCUU ACCACACACUCUC ACCACCUCUU ACCACACACUCUC ACCACCUCUU ACCACACCUCUC ACCACCUCUU ACCACCACCUCUU ACCACACACUCUC ACCACCUCUU ACCACCCUCUCUCAACCACCUC ACCACCUCUU ACCACCCUCUCUCAACCACCUC ACCACCUCUCUCACACCCUC ACACCCUCUCUCAACCCUC ACACACCUCUC ACACCCUCUCUCAACCCUC ACACCCUCUCUCAACCCUC ACACCCUCUCUCAACCCUC ACACCCUCC ACACCCUCCACACCUCC ACACCCUCCACACCUCCACACCCUCCACACCUCCACACCCU	CGAGGUCUC CAUCAGUG
2061 UAAGGUCG CUGAUGA X GAA AGAGCCAC GUGGCUCUA CO 2068 GACAGUCU CUGAUGA X GAA AGAGCCAC 2069 UGACAGUC CUGAUGA X GAA AGGUCGU ACGACCUU AC 2076 UCUAGCUU CUGAUGA X GAA AAGGUCGU ACGACCUUA GA 2076 UCUAGCUU CUGAUGA X GAA ACAGUCUA UAGACCUUA GA 2082 GACACCUC CUGAUGA X GAA ACACUCU AGAGGUGUC AA 2090 GGCGCGGG CUGAUGA X GAA ACACCUCU AGAGGUGUC CU 2100 AGUGAUCU CUGAUGA X GAA ACACCUCU AGAGGUGUC CU 2100 AGUGAUCU CUGAUGA X GAA AUCUGAGG CCUCAGAUC AC 2109 UUUGAACC CUGAUGA X GAA AUCUGAGG CCUCAGAUC AC 2109 UUUGAACC CUGAUGA X GAA ACCAAGUU AGAUCACUU GC 2113 UGUUUUUG CUGAUGA X GAA ACCAAGUU CACUUGGUU CA 2114 UUGUUUUU CUGAUGA X GAA AACCAAGU ACUUGGUUC AA 2132 UCUUGUUG CUGAUGA X GAA AUUUUGUG CACAAAAUA CA 2132 UCUUGUUG CUGAUGA X GAA AUUUCCCGG CCGGGAAUUA AC 2151 UCCUAAAAU CUGAUGA X GAA AUUUCCCGG CCGGGAAUUA AC 2151 UCCUAAAA CUGAUGA X GAA AAUAAUUCC GGGAAUUA UC 2153 GGUCCUAA CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2154 UGGUCCUA CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2156 CCUGGUCC CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2157 UUUCAAUA CUGAUGA X GAA AAUAAUAU AAUUAUUUU AC 2158 CCUGGUCCU CUGAUGA X GAA AAUAAUAU AAUUAUUUU AC 2159 UUUCAAU CUGAUGA X GAA AAAAAAAAAA AUAAUUUC GAAUUAUUU UA 2180 CUUUCAAU CUGAUGA X GAA AAAAAAAAAAAAAAAAAAAAAAAAAAA	GUCUCCAUC AGUGGCUC
2068 GACAGUCU CUGAUGA X GAA AGGUCGUA UACGACCUU AG 2069 UGACAGUC CUGAUGA X GAA AAGGUCGU ACGACCUUA GA 2076 UCUAGCUU CUGAUGA X GAA ACAGUCUA UAGACUGUC AA 2082 GACACCUC CUGAUGA X GAA ACAGUCUA UAGACUGUC AA 2090 GGCGCGGG CUGAUGA X GAA ACACCUCU AGAGGUGUC CO 2100 AGUGAUCU CUGAUGA X GAA ACACCUCU AGAGGUGUC CO 2100 AGUGAUCU CUGAUGA X GAA ACACCUCU AGAGGUGUC CO 2100 AGUGAUCU CUGAUGA X GAA AUCUGAGG CCUCAGAUC AC 2109 UUUGAACC CUGAUGA X GAA AUCUGAGG CCUCAGAUC AC 2113 UGUUUUUG CUGAUGA X GAA ACCAAGUG CACUUGGUU CA 2114 UUGUUUUU CUGAUGA X GAA ACCAAGUG CACUUGGUU CA 2112 UCUUGUUG CUGAUGA X GAA AUUUUGUG CACAAAAUA CA 2132 UCUUGUUG CUGAUGA X GAA AUUUCCCGG CCGGGAAUUA AC 2151 UCCUAAAA CUGAUGA X GAA AUUUCCCGG CCGGGAAUUA UC 2153 GGUCCUAA CUGAUGA X GAA AUAAUUCC GGAAUUAUU UA 2154 UGGUCCUA CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAAAAAUAU AAUUAUUUU AG 2156 CCUGGUCC CUGAUGA X GAA AAAAAAAUAU AAUUAUUUU AG 2157 UUUCAAUA CUGAUGA X GAA AAAAAAAUAU AAUUAUUUU AG 2158 CCUGGUCC CUGAUGA X GAA AAAAAAAAUA AUUAUUUUA GG 2179 UUUCAAUA CUGAUGA X GAA AAAAAAAAUA AUUAUUUUA GG 2180 CUUUCAAU CUGAUGA X GAA AAAAAAAAUA AUUAUUUUA GG 2181 UCUUUCAA CUGAUGA X GAA AAAAAAAAAA CCGCGUGUUU AU 2181 UCUUUCAA CUGAUGA X GAA AAAAAAAAA CCGCGUGUUU AU 2183 ACUCUUUC CUGAUGA X GAA AAAAAAAAAAAAAAAAAAAAAAAAAAA	CAGUGGCUC UACGACCU
10 2069 UGACAGUC CUGAUGA X GAA AAGGUCGU ACGACCUUA GA 2076 UCUAGCUU CUGAUGA X GAA ACAGUCUA UAGACUGUC AA 2082 GACACCUC CUGAUGA X GAA ACACUCU AGAGGUGUC CU 2090 GGCGCGGG CUGAUGA X GAA ACACCUCU AGAGGUGUC CO 2100 AGUGAUCU CUGAUGA X GAA ACACCUCU AGAGGUGUC CO 2100 AGUGAUCU CUGAUGA X GAA ACACCUCU AGAGGUGUC CO 2100 UUUGAACC CUGAUGA X GAA AUCUGAGG CCCUCAGAUC AC 2109 UUUGAACC CUGAUGA X GAA AUCUGAGG CACUUGGUU CA 2113 UGUUUUU CUGAUGA X GAA ACCAAGUG CACUUGGUU CA 2114 UUGUUUUU CUGAUGA X GAA ACCAAGUG CACUUGGUU CA 2115 UCUUGUUG CUGAUGA X GAA AUUUUGUG CACAAAAUA CA 2132 UCUUGUUG CUGAUGA X GAA AUUUCCCGG CCGGGAAUUA CU 2151 UCCUAAAA CUGAUGA X GAA AUUCCCGG CCGGGAAUUA CU 2153 GGUCCUAA CUGAUGA X GAA AUAAUUCC GGAAUUAUUU UA 2154 UGGUCCUA CUGAUGA X GAA AUAAUUCC GGAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAAAAAAUA AUUAUUUU AA 2156 CUGGUCC CUGAUGA X GAA AAAAAAAUA AUUAUUUUA GC 2179 UUUCAAUA CUGAUGA X GAA AAAAAAAUA AUUAUUUUA GC 2180 CUUUCAAU CUGAUGA X GAA AAAAAAAAUA AUUAUUUUA GC 2181 UCUUUCAA CUGAUGA X GAA AAAAAAAAA CACCCCUC GCCCCGUUUUA CU 2181 UCUUUCAA CUGAUGA X GAA AAAAAAAAA CCCCCUC GCCCCCUUUUA CCCCCCCCCC	GUGGCUCUA CGACCUUA
2076 UCUAGCUU CUGAUGA X GAA ACAGUCUA UAGACUGUC AA 2082 GACACCUC CUGAUGA X GAA AGCUUGAC GUCAAGCUA GA 2090 GGCGCGGG CUGAUGA X GAA AGCUUGAC 2100 AGUGAUCU CUGAUGA X GAA AGCCCCCU AGAGGUGUC CC 2100 AGUGAUCU CUGAUGA X GAA AGCCCCCC AGAUCACCUC 2109 UUUGAACC CUGAUGA X GAA AUCUGAGG CCUCCAGAUC AC 2113 UGUUUUUG CUGAUGA X GAA ACCCAAGU AGAUCACUU GC 2114 UUGUUUUU CUGAUGA X GAA ACCAAGU ACUUGGUUC AA 2114 UUGUUUUU CUGAUGA X GAA AACCAAGU ACUUGGUUC AA 2132 UCUUGUUG CUGAUGA X GAA AUUUUGUG CACAAAAUA CA 2132 UCUUGUUG CUGAUGA X GAA AUUUCCCGG CCGGGAAUUA UC 2151 UCCUAAAA CUGAUGA X GAA AUUCCCGG CCGGGAAUUA UC 2153 GGUCCUAA CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2154 UGGUCCUA CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAAAAAUAAU AAUUAUUUU AA 2156 CCUGGUCC CUGAUGA X GAA AAAAAAUAAU AAUUAUUUU AA 2157 UUUCAAUA CUGAUGA X GAA AAAAAAAUA AUUAUUUUUA GC 2179 UUUCAAUA CUGAUGA X GAA AAAAAAAUA AUUAUUUUU AC 2180 CUUUCAAU CUGAUGA X GAA AAAAAAAUA AUUAUUUUUA GC 2181 UCUUUCAAU CUGAUGA X GAA AAAAAAAAUA AUUAUUUUUA GC 2181 UCUUUCAAU CUGAUGA X GAA AAAAAAACAG CACCCUGUUU AU 2183 ACUCUUUC CUGAUGA X GAA AAAAAACAG CACCCUUUUA CC 2183 ACUCUUUC CUGAUGA X GAA AAAAAAAAAAAAAAAAAAAAAAAAAAA	UACGACCUU AGACUGUC
2082 GACACCUC CUGAUGA X GAA AGCUUGAC GUCAAGCUA GA 2090 GGCGCGGG CUGAUGA X GAA ACACCUCU AGAGGUGC CC 2100 AGUGAUCU CUGAUGA X GAA AGCCGGG CCCGCGCCUC AG 2100 AGUGAUCU CUGAUGA X GAA AUCUGAGG CCUCCAGAUC AC 2109 UUUGAACC CUGAUGA X GAA AGUGAUCU AGAUCACUU GG 2113 UGUUUUUG CUGAUGA X GAA ACCAAGUG CACUUGGUU CA 2114 UUGUUUUU CUGAUGA X GAA AACCAAGU ACUUGGUUC AA 2132 UCUUGUUG CUGAUGA X GAA AUUUUGUG CACAAAAUA CA 2132 UCUUGUUG CUGAUGA X GAA AUUUUGUG CACAAAAUA CA 2151 UCCUAAAA CUGAUGA X GAA AUUCCCGG CCGGGAAUUA UC 2151 UCCUAAAA CUGAUGA X GAA AAUAAUUCC GGAAUUAUU UC 2153 GGUCCUAA CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAAAAAAUA 2179 UUUCAAUA CUGAUGA X GAA AAAAAAAUAAU AUUAUUUUA GG 2179 UUUCAAUA CUGAUGA X GAA AAAAAAAUAAU AUUAUUUUUA GG 2180 CUUUCAAU CUGAUGA X GAA AAAAAAAAAA CCGCGUGUUU UA 2181 UCUUUCAA CUGAUGA X GAA AAAAAAAAAAAAAAAAAAAAAAAAAAA	ACGACCUUA GACUGUCA
2090 GGCGCGGG CUGAUGA X GAA ACACCUCU AGAGGUGUC CC 2100 AGUGAUCU CUGAUGA X GAA AGCCGCGG CCCGCGCCUC AG 2100 AGUGAUCU CUGAUGA X GAA AUCUGAGG CCUCAGAUC AC 2109 UUUGAACC CUGAUGA X GAA AGUGAUCU AGAUCACUU GC 2113 UGUUUUUU CUGAUGA X GAA ACCAAGU ACUUGGUUC AA 2114 UUGUUUUU CUGAUGA X GAA AACCAAGU ACUUGGUUC AA 2132 UCUUGUUG CUGAUGA X GAA AUUUUGUG CACAAAAUA CA 2150 CCUAAAAU CUGAUGA X GAA AUUUCCCGG CCGGGAAUU AU 2151 UCCUAAAA CUGAUGA X GAA AAUACCCG CGGGAAUUA UC 2153 GGUCCUAA CUGAUGA X GAA AAUAAUUC GGAAUUAUUU UA 2154 UGGUCCUA CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAAAAAAUA AUUAUUUUA GG 2156 CCUGGUCC CUGAUGA X GAA AAAAAAAAUA AUUAUUUUA GG 2179 UUUCAAUA CUGAUGA X GAA AAAAAAAAUA AUUAUUUUA GG 2179 UUUCAAUA CUGAUGA X GAA AAAAAAAAA AAAAAAAAAAAAAAAAA	UAGACUGUC AAGCUAGA
2100 AGUGAUCU CUGAUGA X GAA AGGCGCGG CCGCGCCUC AGG 15 2105 AACCAAGU CUGAUGA X GAA AUCUGAGG CCUCAGAUC AC 2109 UUUGAACC CUGAUGA X GAA AUCUGAGG CACUUGGUU CA 2113 UGUUUUU CUGAUGA X GAA ACCAAGUG CACUUGGUU CA 2114 UUGUUUUU CUGAUGA X GAA AACCAAGU ACUUGGUUC AA 2132 UCUUGUUG CUGAUGA X GAA AUUUUGUG CACAAAAUA CA 2150 CCUAAAAU CUGAUGA X GAA AUUUCCCGG CCGGGAAUUA UU 2151 UCCUAAAA CUGAUGA X GAA AAUACCCG CGGGAAUUA UU 2153 GGUCCUAA CUGAUGA X GAA AAUAAUUCC GGAAUUAUU UU 2154 UGGUCCU CUGAUGA X GAA AAAAAUAAUU AAUUAUUUU AC 2155 CUGGUCCU CUGAUGA X GAA AAAAAAAUA AUUAUUUUU AC 2156 CCUGGUCC CUGAUGA X GAA AAAAAAAAU AUUAUUUUU AC 2179 UUUCAAUA CUGAUGA X GAA AAAAAAAAU AUUAUUUUU AC 2180 CUUUCAAU CUGAUGA X GAA AAAAAAAAU AUUAUUUU AC 2181 UCUUUCAA CUGAUGA X GAA AAAAAAAAU AUUAUUUU AC 2181 UCUUUCAA CUGAUGA X GAA AAAAAAAAA AAAAAAAAAAAAAAAAA	GUCAAGCUA GAGGUGUC
2105 AACCAAGU CUGAUGA X GAA AUCUGAGG CCUCAGAUC AC 2109 UUUGAACC CUGAUGA X GAA AGUGAUCU AGAUCACUU GG 2113 UGUUUUU CUGAUGA X GAA ACCAAGUG CACUUGGUU CA 2114 UUGUUUUU CUGAUGA X GAA AACCAAGU ACUUGGUUC AA 2132 UCUUGUUG CUGAUGA X GAA AUUUUGUG CACAAAAUA CA 2150 CCUAAAAU CUGAUGA X GAA AUUUCCCGG CCGGGAAUUA UU 2151 UCCUAAAA CUGAUGA X GAA AAUAAUUCC GGAAUUAUU UU 2153 GGUCCUAA CUGAUGA X GAA AAUAAUUCC GGAAUUAUU UU 2154 UGGUCCUA CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAAAAAUAAU AAUUAUUUU AA 2156 CCUGGUCC CUGAUGA X GAA AAAAAAAUA AUUAUUUU AA 2179 UUUCAAUA CUGAUGA X GAA AAAAAAAAUA AUUAUUUUA GG 2179 UUUCAAUA CUGAUGA X GAA AAAAAAAAUA AUUAUUUU AA 2180 CUUUCAAU CUGAUGA X GAA AAAAAAAAUA AUAAUUC GACCUGUUU AAU 2181 UCUUUCAA CUGAUGA X GAA AAAAAAAAAAAAAAAAAAAAAAAAAAA	AGAGGUGUC CCCGCGCC
2109 UUUGAACC CUGAUGA X GAA AGUGAUCU AGAUCACUU GG 2113 UGUUUUUG CUGAUGA X GAA ACCAAGUG CACUUGGUU CA 2114 UUGUUUUU CUGAUGA X GAA AACCAAGU ACUUGGUUC AA 2132 UCUUGUUG CUGAUGA X GAA AUUUUGUG CACAAAAUA CA 2150 CCUAAAAU CUGAUGA X GAA AUUCCCGG CCGGGAAUUA UU 2151 UCCUAAAA CUGAUGA X GAA AAUUCCCG CGGGAAUUA UU 2153 GGUCCUAA CUGAUGA X GAA AAUAAUUCC GGAAUUAUU UU 2154 UGGUCCUA CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAAUAAUU AAUUAUUUU AA 2156 CCUGGUCC CUGAUGA X GAA AAAAAAAUA AUUAUUUUA GG 2179 UUUCAAUA CUGAUGA X GAA AAAAAAAAUA AUUAUUUUA GG 2180 CUUUCAAU CUGAUGA X GAA ACACGCGU CACGCUGUU UA 2181 UCUUUCAA CUGAUGA X GAA AACAGCGU ACGCUGUUU AU 2183 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2183 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UC 2183 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UC 2181 UCCUCUGU CUGAUGA X GAA AAACAGCG CGCUGUUUA UC 2182 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UC 2183 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UC 2184 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UC 2185 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UC 2181 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UC 2181 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UC 2183 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UC 2184 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UC 2185 ACUCUUUC CUGAUGA X GAA ACACCCCC GAAGGUGC UAAAACAG CUGAUGAU X GAA ACACCCCUC GAAGGUGUC UAAAACAG COGCUGUUUA UC 2213 CACCUAUA CUGAUGA X GAA ACACCCCC GAGGGUGUC UAAAACAG COGCUGUUUA UC	CCGCGCCUC AGAUCACU
2113 UGUUUUUG CUGAUGA X GAA ACCAAGUG CACUUGGUU CA 2114 UUGUUUUU CUGAUGA X GAA AACCAAGU ACUUGGUUC AA 2132 UCUUGUUG CUGAUGA X GAA AUUUUGUG CACAAAAUA CA 2132 UCUUGUUG CUGAUGA X GAA AUUUCCCGG CCGGGAAUU AU 2150 CCUAAAAU CUGAUGA X GAA AUUCCCGG CCGGGAAUUA UU 2151 UCCUAAAA CUGAUGA X GAA AAUAAUUCC GGAAUUAUU UU 2153 GGUCCUAA CUGAUGA X GAA AAAAAUAAUU GAAAUAAUU UU 2154 UGGUCCU CUGAUGA X GAA AAAAAAAUU AAUUAUUUU AG 2155 CUGGUCCU CUGAUGA X GAA AAAAAAAU AUUAUUUU AG 2179 UUUCAAAU CUGAUGA X GAA AAAAAAAU AUUAUUUUA GG 2179 UUUCAAU CUGAUGA X GAA AACAGCGU CACGCUGUU UA 2180 CUUUCAAU CUGAUGA X GAA AACAGCGU ACGCUGUUU AU 2181 UCUUUCAA CUGAUGA X GAA AACAGCGU CGCUGUUUA UU 2183 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2183 ACUCUUUC CUGAUGA X GAA AACAGCGG CGCUGUUUA UU 2181 UCUUUCAA CUGAUGA X GAA AACAGCG CGCUGUUUA UU 2181 ACUCUUUC CUGAUGA X GAA ACACCCUC GAAAGAGCC UG	CCUCAGAUC ACUUGGUU
2114 UUGUUUUU CUGAUGA X GAA AACCAAGU ACUUGGUUC AA 2132 UCUUGUUG CUGAUGA X GAA AUUUUGUG CACAAAAUA CA 20 2150 CCUAAAAU CUGAUGA X GAA AUUCCCGG CCGGGAAUU AU 2151 UCCUAAAA CUGAUGA X GAA AAUUCCCG CGGGAAUUA UU 2153 GGUCCUAA CUGAUGA X GAA AAUAAUUCC GGAAUUAUU UU 2154 UGGUCCUA CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAAAAAUAAU AAUUAUUUU AA 2156 CCUGGUCC CUGAUGA X GAA AAAAAAAUA AUUAUUUUUA GG 2179 UUUCAAUA CUGAUGA X GAA AAAAAAAUAAU AUUAUUUUUA 2180 CUUUCAAU CUGAUGA X GAA AACAGCGU CACGCUGUU UA 2181 UCUUUCAA CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2183 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2183 ACUCUUUC CUGAUGA X GAA AAACAGCG CUGUUUUAUU GA 30 2192 UCCUCUGU CUGAUGA X GAA ACACCCUC GAAGAGUC AC 2213 CACCUAUA CUGAUGA X GAA ACACCCUC GAGGGUGUC UA 2215 GGCACCUA CUGAUGA X GAA ACACCCUC GAGGGUGUC UA	AGAUCACUU GGUUCAAA
2132 UCUUGUUG CUGAUGA X GAA AUUUUGUG CACAAAAUA CA 20 2150 CCUAAAAU CUGAUGA X GAA AUUCCCGG CCGGGAAUU AU 2151 UCCUAAAA CUGAUGA X GAA AAUUCCCG CGGGAAUUA UU 2153 GGUCCUAA CUGAUGA X GAA AAUAAUUCC GGAAUUAUU UU 2154 UGGUCCUA CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAAAAAUAU AAUUAUUUU AG 2156 CCUGGUCC CUGAUGA X GAA AAAAAAAUAAU AUUAUUUUA GG 2179 UUUCAAUA CUGAUGA X GAA AACAGCGU CACGCUGUU UA 2180 CUUUCAAU CUGAUGA X GAA AACAGCGU ACGCUGUUU AU 2181 UCUUUCAA CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2183 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2183 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2181 UCCUCUGU CUGAUGA X GAA AAAACAG CUGUUUAUU GA 30 2192 UCCUCUGU CUGAUGA X GAA ACACCCCC GAAGAGGUC UA 2213 CACCUAUA CUGAUGA X GAA ACACCCCC GAGGGUGUC UA 2215 GGCACCUA CUGAUGA X GAA ACACCCCC GAGGGUGUC UA	CACUUGGUU CAAAAACA
20 2150 CCUAAAAU CUGAUGA X GAA AUUCCCGG CCGGGAAUU AU 2151 UCCUAAAA CUGAUGA X GAA AAUUCCCG CGGGAAUUA UU 2153 GGUCCUAA CUGAUGA X GAA AUAAUUCC GGAAUUAUU UA 2154 UGGUCCUA CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAAUAAUU AAUUAUUUU AG 2179 UUUCAAUA CUGAUGA X GAA AAAAUAAU AUUAUUUUA GG 2179 UUUCAAUA CUGAUGA X GAA AACAGCGU CACGCUGUU UA 2180 CUUUCAAU CUGAUGA X GAA AACAGCGU ACGCUGUUU AU 2181 UCUUUCAA CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2183 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2183 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2181 UCCUCUGU CUGAUGA X GAA AACAGCGC CGCUGUUUA UU 2182 ACCCUAUA CUGAUGA X GAA ACCCCUC GAAGAGGUC AC 2213 CACCUAUA CUGAUGA X GAA ACACCCUC GAGGGUGUC UA 2215 GGCACCUA CUGAUGA X GAA ACACCCUC GAGGGUGUC UA	ACUUGGUUC AAAAACAA
2151 UCCUAAAA CUGAUGA X GAA AAUUCCCG CGGGAAUUA UU 2153 GGUCCUAA CUGAUGA X GAA AUAAUUCC GGAAUUAUU UU 2154 UGGUCCUA CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAAUAAUU AAUUAUUUU AG 2156 CCUGGUCC CUGAUGA X GAA AAAAUAAU AUUAUUUUA GG 2179 UUUCAAUA CUGAUGA X GAA ACAGCGUG CACGCUGUU UA 2180 CUUUCAAU CUGAUGA X GAA AACAGCGU ACGCUGUUU AU 2181 UCUUUCAA CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2183 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2183 ACUCUUUC CUGAUGA X GAA AUAAACAG CUGUUUAUU GA 30 2192 UCCUCUGU CUGAUGA X GAA ACCCCUC GAGGGUGUC UA 2215 GGCACCUA CUGAUGA X GAA ACACCCUC GAGGGUGUC UA	CACAAAAUA CAACAAGA
2153 GGUCCUAA CUGAUGA X GAA AUAAUUCC GGAAUUAUU UZ 2154 UGGUCCUA CUGAUGA X GAA AAUAAUUC GAAUUAUUU UZ 2155 CUGGUCCU CUGAUGA X GAA AAAUAAUU AAUUAUUUU AG 2179 UUUCAAUA CUGAUGA X GAA ACAGCGUG CACGCUGUU UZ 2180 CUUUCAAU CUGAUGA X GAA AACAGCGU ACGCUGUUU AU 2181 UCUUUCAA CUGAUGA X GAA AAACAGCG CGCUGUUUA UZ 2183 ACUCUUUC CUGAUGA X GAA AAACAGCG CGCUGUUUA UZ 2183 ACUCUUUC CUGAUGA X GAA AUAAACAG CUGUUUAUU GA 30 2192 UCCUCUGU CUGAUGA X GAA ACCCCUC GAAGAGUC AC 2213 CACCUAUA CUGAUGA X GAA ACACCCUC GAGGGUGUC UZ 2215 GGCACCUA CUGAUGA X GAA AGACACCC GGGUGUCUA UZ	CCGGGAAUU AUUUUAGG
2154 UGGUCCUA CUGAUGA X GAA AAUAAUUC GAAUUAUUU UA 2155 CUGGUCCU CUGAUGA X GAA AAAAUAAUU AAUUAUUUU AG 2156 CCUGGUCC CUGAUGA X GAA AAAAUAAU AUUAUUUUUA GG 2179 UUUCAAUA CUGAUGA X GAA ACAGCGUG CACGCUGUU UA 2180 CUUUCAAU CUGAUGA X GAA AACAGCGU ACGCUGUUU AU 2181 UCUUUCAA CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2183 ACUCUUUC CUGAUGA X GAA AUAAACAG CUGUUUUAUU GA 30 2192 UCCUCUGU CUGAUGA X GAA ACCCCUC GAAGAGUC AC 2213 CACCUAUA CUGAUGA X GAA ACACCCUC GAGGGUGUC UA 2215 GGCACCUA CUGAUGA X GAA AGACACCC GGGUGUCUA UA	CGGGAAUUA UUUUAGGA
2155 CUGGUCCU CUGAUGA X GAA AAAUAAUU AAUUAUUUU AG 25 2156 CCUGGUCC CUGAUGA X GAA AAAAUAAU AUUAUUUUA GG 2179 UUUCAAUA CUGAUGA X GAA ACAGCGUG CACGCUGUU UA 2180 CUUUCAAU CUGAUGA X GAA AACAGCGU ACGCUGUUU AU 2181 UCUUUCAA CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2183 ACUCUUUC CUGAUGA X GAA AUAAACAG CUGUUUUAUU GA 30 2192 UCCUCUGU CUGAUGA X GAA ACCCCUC GAAGAGGUC AC 2213 CACCUAUA CUGAUGA X GAA ACACCCUC GAGGGUGUC UA 2215 GGCACCUA CUGAUGA X GAA AGACACCC GGGUGUCUA UA	GGAAUUAUU UUAGGACC
25 2156 CCUGGUCC CUGAUGA X GAA AAAAUAAU AUUAUUUUA GG 2179 UUUCAAUA CUGAUGA X GAA ACAGCGUG CACGCUGUU UA 2180 CUUUCAAU CUGAUGA X GAA AACAGCGU ACGCUGUUU AU 2181 UCUUUCAA CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2183 ACUCUUUC CUGAUGA X GAA AUAAACAG CUGUUUAUU GA 30 2192 UCCUCUGU CUGAUGA X GAA ACUCUUUC GAAAGAGUC AC 2213 CACCUAUA CUGAUGA X GAA ACACCCUC GAGGGUGUC UA	GAAUUAUUU UAGGACCA
2179 UUUCAAUA CUGAUGA X GAA ACAGCGUG CACGCUGUU UA 2180 CUUUCAAU CUGAUGA X GAA AACAGCGU ACGCUGUUU AU 2181 UCUUUCAA CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2183 ACUCUUUC CUGAUGA X GAA AUAAACAG CUGUUUAUU GA 30 2192 UCCUCUGU CUGAUGA X GAA ACUCUUUC GAAAGAGUC AC 2213 CACCUAUA CUGAUGA X GAA ACACCCUC GAGGGUGUC UA 2215 GGCACCUA CUGAUGA X GAA AGACACCC GGGUGUCUA UA	AAUUAUUUU AGGACCAG
2180 CUUUCAAU CUGAUGA X GAA AACAGCGU ACGCUGUUU AU 2181 UCUUUCAA CUGAUGA X GAA AAACAGCG CGCUGUUUA UU 2183 ACUCUUUC CUGAUGA X GAA AUAAACAG CUGUUUAUU GA 30 2192 UCCUCUGU CUGAUGA X GAA ACUCUUUC GAAAGAGUC AC 2213 CACCUAUA CUGAUGA X GAA ACACCCUC GAGGGUGUC UA 2215 GGCACCUA CUGAUGA X GAA AGACACCC GGGUGUCUA UA	AUUAUUUUA GGACCAGG
2181 UCUUUCAA CUGAUGA X GAA AAACAGCG CGCUGUUUA UC 2183 ACUCUUUC CUGAUGA X GAA AUAAACAG CUGUUUAUU GA 30 2192 UCCUCUGU CUGAUGA X GAA ACUCUUUC GAAAGAGUC AC 2213 CACCUAUA CUGAUGA X GAA ACACCCUC GAGGGUGUC UA 2215 GGCACCUA CUGAUGA X GAA AGACACCC GGGUGUCUA UA	CACGCUGUU UAUUGAAA
2183 ACUCUUUC CUGAUGA X GAA AUAAACAG CUGUUUAUU GA 30 2192 UCCUCUGU CUGAUGA X GAA ACUCUUUC GAAAGAGUC AC 2213 CACCUAUA CUGAUGA X GAA ACACCCUC GAGGGUGUC UA 2215 GGCACCUA CUGAUGA X GAA AGACACCC GGGUGUCUA UA	ACGCUGUUU AUUGAAAG
30 2192 UCCUCUGU CUGAUGA X GAA ACUCUUUC GAAAGAGUC AC 2213 CACCUAUA CUGAUGA X GAA ACACCCUC GAGGGUGUC UA 2215 GGCACCUA CUGAUGA X GAA AGACACCC GGGUGUCUA UA	CGCUGUUUA UUGAAAGA
2213 CACCUAUA CUGAUGA X GAA ACACCCUC GAGGGUGUC UA 2215 GGCACCUA CUGAUGA X GAA AGACACCC GGGUGUCUA UA	CUGUUUAUU GAAAGAGU
2215 GGCACCUA CUGAUGA X GAA AGACACCC GGGUGUCUA UA	GAAAGAGUC ACAGAGGA
••••	GAGGGUGUC UAUAGGUG
2217 UCGGCACC CUGAUGA X GAA AUAGACAC GUGUGUANA GO	GGGUGUCUA UAGGUGCC
GOOCOACA GO	GUGUCUAUA GGUGCCGA

	2263	CGGUGAG	G CUGAUGA	A :	X GA	A AGGCUGCG	CGCAGCCUA CCUCACCG
	2267	UGCACGGI	J CUGAUGA	A :	X GA	A AGGUAGGC	GCCUACCUC ACCGUGCA
	2284	ACUUGUC	J CUGAUGA		X GA	A AGGUUCCU	AGGAACCUC AGACAAGU
	2293	CCAGGUUT	J CUGAUGA		K GA	A ACUUGUCU	AGACAAGUC AAACCUGG
5	2309	GUGAGCGU	J CUGAUGA		(GA	A AUCAGCUC	GAGCUGAUC ACGCUCAC
	2315	GUGCACGU	J CUGAUGA	. 3	GA/	A AGCGUGAU	AUCACGCUC ACGUGCAC
	2342	AGCCAAAA	CUGAUGA	. 2	GA,	A AGGGUCGC	GCGACCCUC UUUUGGCU
	2344	GGAGCCAA	CUGAUGA	. }	GA,	AGAGGGUC	GACCCUCUU UUGGCUCC
٠	2345	AGGAGCCA	CUGAUGA	. }	GA#	AAGAGGGU	ACCCUCUUU UGGCUCCU
10	2346	AAGGAGCC	CUGAUGA	. >	GAA	AAAGAGGG	CCCUCUUUU GGCUCCUU
	2351	GUUAGAAG	CUGAUGA	X	GAA	AGCCAAAA	UUUUGGCUC CUUCUAAC
	2354	AGAGUUAG	CUGAUGA	X	GAA	AGGAGCCA	UGGCUCCUU CUAACUCU
	2355	GAGAGUUA	CUGAUGA	Х	GAA	AAGGAGCC	GGCUCCUUC UAACUCUC
	2357	AAGAGAGU	CUGAUGA	X	GAA	AGAAGGAG	CUCCUUCUA ACUCUCUU
15	2361	GAUGAAGA	CUGAUGA	Х	GAA	AGUUAGAA	UUCUAACUC UCUUCAUC
	23 63	CUGAUGAA	CUGAUGA	Х	GAA	AGAGUUAG	CUAACUCUC UUCAUCAG
	236 5	UUCUGAUG	CUGAUGA	Х	GAA	AGAGAGUU	AACUCUCUU CAUCAGAA
	236 6	UUUCUGAU	CUGAUGA	Х	GAA	AAGAGAGU	ACUCUCUUC AUCAGAAA
	2369	AGUUUUCU	CUGAUGA	Х	GAA	AUGAAGAG	CUCUUCAUC AGAAAACU
20	2386	CGGAAGAA	CUGAUGA	X	GAA	ACCGCUUC	GAAGCGGUC UUCUUCCG
	2388	UUCGGAAG	CUGAUGA	X	GAA	AGACCGCU	AGCGGUCUU CUUCCGAA
	2389	CUUCGGAA	CUGAUGA	Х	GAA	AAGACCGC	GCGGUCUUC UUCCGAAG
	2391	UACUUCGG	CUGAUGA	X	GAA	AGAAGACC	GGUCUUCUU CCGAAGUA
	2392	UUACUUCG	CUGAUGA	X	GAA	AAGAAGAC	GUCUUCUUC CGAAGUAA
25	2399	UCUGUCUU	CUGAUGA	X	GAA	ACUUCGGA	UCCGAAGUA AAGACAGA
	2410	UUGACAGG	CUGAUGA	X	GAA	AGUCUGUC	GACAGACUA CCUGUCAA
	2416	UAAUGAUU	CUGAUGA	X	GAA	ACAGGUAG	CUACCUGUC AAUCAUUA
	2420	UCCAUAAU	CUGAUGA	Х	GAA	AUUGACAG	CUGUCAAUC AUUAUGGA
	2423	GGGUCCAU	CUGAUGA	X	GAA	AUGAUUGA	UCAAUCAUU AUGGACCC
30	2424	UGGGUCCA	CUGAUGA	x	GAA	AAUGAUUG	CAAUCAUUA UGGACCCA
	2441	UCCAGGGG	CUGAUGA	X	GAA	ACUUCAUC	GAUGAAGUU CCCCUGGA
	2442	AUCCAGGG	CUGAUGA	х	GAA	AACUUCAU	AUGAAGUUC CCCUGGAU
	2473	UGGCAUCA	CUGAUGA	X	GAA	AGGGCAGC	GCUGCCCUA UGAUGCCA

	2494	CCCGUGCA	CUGAUGA	. X	GAA	ACUCCCAC	GUGGGAGUU	UGCACGG
	2495	UCCCGUGC	CUGAUGA	X	GAA	AACUCCCA	UGGGAGUUU	GCACGGGA
	2516	GAUUUGCC	CUGAUGA	X	GAA	AGUUUCAG	CUGAAACUA	GGCAAAUC
	2524	UUCCGAGC	CUGAUGA	Х	GAA	AUUUGCCU	AGGCAAAUC	GCUCGGAA
5	2528	CCUCUUCC	CUGAUGA	X	GAA	AGCGAUUU	AAAUCGCUC	GGAAGAGG
	2541	UUUCCCAA	CUGAUGA	Х	GAA	AGCCCCUC	GAGGGGCUU	UUGGGAAA
	2542	CUUUCCCA	CUGAUGA	X	GAA	AAGCCCCU	AGGGGCUUU	UGGGAAAG
	2543	ACUUUCCC	CUGAUGA	X	GAA	AAAGCCCC	GGGGCUUUU	GGGAAAGU
	2552	GCUUGAAC	CUGAUGA	X	GAA	ACUUUCCC	GGGAAAGUC	GUUCAAGC
10	2555	GAGGCUUG	CUGAUGA	Х	GAA	ACGACUUU	AAAGUCGUU	CAAGCCUC
	2556	AGAGGCUU	CUGAUGA	X	GAA	AACGACUU	AAGUCGUUC	AAGCCUCU
	256 3	CAAAUGCA	CUGAUGA	Х	GAA	AGGCUUGA	UCAAGCCUC	UGCAUUUG
	2569	UAAUGCCA	CUGAUGA	X	GAA	AUGCAGAG	CUCUGCAUU	UGGCAUUA
	2570	UUAAUGCC	CUGAUGA	X	GAA	AAUGCAGA	UCUGCAUUU	GGCAUUAA
1 5	2576	GAUUUCUU	CUGAUGA	X	GAA	AUGCCAAA	UUUGGCAUU	AAGAAAUC
	2577	UGAUUUCU	CUGAUGA	X	GAA	AAUGCCAA	UUGGCAUUA	AGAAAUCA
	2584	AGGUGGGU	CUGAUGA	X	GAA	AUUUCUUA	UAAGAAAUC	ACCCACCU
	2617	CCUCUUUC	CUGAUGA	Х	GAA	ACAUCUUC	GAAGAUGUU	GAAAGAGG
	2644	GAGCUUUG	CUGAUGA	X	GAA	ACUCACUG	CAGUGAGUA	CAAAGCUC
20	2652	GGUCAUCA	CUGAUGA	X	GAA	AGCUUUGU	ACAAAGCUC	UGAUGACC
	2666	AAGAUCUU	CUGAUGA	Х	GAA	AGUUCGGU	ACCGAACUC	AAGAUCUU
	2672	UGGGUCAA	CUGAUGA	X	GAA	AUCUUGAG	CUCAAGAUC	UUGACCCA
	2674	UGUGGGUC	CUGAUGA	X	GAA	AGAUCUUG	CAAGAUCUU	GACCCACA
	2684	UGAUGGCC	CUGAUGA	X	GAA	AUGUGGGU	ACCCACAUC	GGCCAUCA
25	2691	AUUCAGAU	CUGAUGA	X	GAA	AUGGCCGA	UCGGCCAUC	AUCUGAAU
	2694	CACAUUCA	CUGAUGA	Х	GAA	AUGAUGGC	GCCAUCAUC	UGAAUGUG
	270 5	AGGAGGUU	CUGAUGA	X	GAA	ACCACAUU	AAUGUGGUU	AACCUCCU
	2706	CAGGAGGU	CUGAUGA	X	GAA	AACCACAU	AUGUGGUUA	ACCUCCUG
	2711	GCUCCCAG	CUGAUGA	X	GAA	AGGUUAAC	GUUAACCUC	CUGGGAGC
30	2742	CACCAUCA	CUGAUGA	Х	GAA	AGGCCCUC	GAGGGCCUC	UGAUGGUG
	27 53	UAUUCCAC	CUGAUGA	X	GAA	AUCACCAU	AUGGUGAUC	GUGGAAUA
	2761	AUUUGCAG	CUGAUGA	X	GAA	AUUCCACG	CGUGGAAUA	CUGCAAAU
	2770	GGUUUCCG	CUGAUGA	Х	GAA	AUUUGCAG	CUGCAAAUA	CGGAAACC

WO 97/15662

	2782	GGUAGUUG	CUGAUGA		K GAA	A ACAGGUUU	AAACCUGUC CAACUACC
	2788	UCUUGAGO	G CUGAUGA	. 2	GA,	AGUUGGAC	GUCCAACUA CCUCAAGA
	2792	uugcucut	J CUGAUGA	. }	GA,	AGGUAGUU	AACUACCUC AAGAGCAA
	28 09	GACAGAAU	J CUGAUGA	. }	GA,	AGUCACGU	ACGUGACUU AUUCUGUC
5	2810	AGACAGAA	CUGAUGA	. >	GAA	AAGUCACG	CGUGACUUA UUCUGUCU
	2812	UGAGACAG	CUGAUGA	X	GAA	AUAAGUCA	UGACUUAUU CUGUCUCA
	2813	UUGAGACA	CUGAUGA	X	GAA	AAUAAGUC	GACUUAUUC UGUCUCAA
	2817	CUUGUUGA	CUGAUGA	Х	GAA	ACAGAAUA	UAUUCUGUC UCAACAAG
	2819	UCCUUGUU	CUGAUGA	Х	GAA	AGACAGAA	UUCUGUCUC AACAAGGA
10	2836	CCAUAUGC	CUGAUGA	Х	GAA	AGGCUGCG	CGCAGCCUU GCAUAUGG
	2841	GAGCUCCA	CUGAUGA	Х	GAA	AUGCAAGG	CCUUGCAUA UGGAGCUC
	2849	ucuuucuu	CUGAUGA	Х	GAA	AGCUCCAU	AUGGAGCUC AAGAAAGA
	2900	ACACUGUC	CUGAUGA	X	GAA	AGGCGGGG	CCCCGCCUA GACAGUGU
	290 9	GAGCUGCU	CUGAUGA	Х	GAA	ACACUGUC	GACAGUGUC AGCAGCUC
15	2917	UGACACUU	CUGAUGA	X	GAA	AGCUGCUG	CAGCAGCUC AAGUGUCA
	2924	GAGCUGGU	CUGAUGA	X	GAA	ACACUUGA	UCAAGUGUC ACCAGCUC
	2932	GGAAGCUG	CUGAUGA	X	GAA	AGCUGGUG	CACCAGCUC CAGCUUCC
	2938	CUUCAGGG	CUGAUGA	X	GAA	AGCUGGAG	CUCCAGCUU CCCUGAAG
	29 39	UCUUCAGG	CUGAUGA	X	GAA	AAGCUGGA	UCCAGCUUC CCUGAAGA
20	2982	CUCACUGU	CUGAUGA	X	GAA	AUCCUCGU	ACGAGGAUU ACAGUGAG
	2983	UCUCACUG	CUGAUGA	X	GAA	AAUCCUCG	CGAGGAUUA CAGUGAGA
	29 93	UGCUUGGA	CUGAUGA	Х	GAA	AUCUCACU	AGUGAGAUC UCCAAGCA
	2995	GCUGCUUG	CUGAUGA	X	GAA	AGAUCUCA	UGAGAUCUC CAAGCAGC
	3008	UCCAUGGU	CUGAUGA	X	GAA	AGGGGCUG	CAGCCCCUC ACCAUGGA
25	3026	CUGUAGGA	CUGAUGA	X	GAA	AUCAGGUC	GACCUGAUU UCCUACAG
	3027	ACUGUAGG	CUGAUGA	X	GAA	AAUCAGGU	ACCUGAUUU CCUACAGU
	3028	AACUGUAG	CUGAUGA	X	GAA	AAAUCAGG	CCUGAUUUC CUACAGUU
	3031	GGAAACUG	CUGAUGA	X	GAA	AGGAAAUC	GAUUUCCUA CAGUUUCC
	3036	CACUUGGA	CUGAUGA	X	GAA	ACUGUAGG	CCUACAGUU UCCAAGUG
30	3037	CCACUUGG	CUGAUGA	X	GAA	AACUGUAG	CUACAGUUU CCAAGUGG
	3038	GCCACUUG	CUGAUGA	Х	GAA	AAACUGUA	UACAGUUUC CAAGUGGC
	3061	AGGACAGA	CUGAUGA :	Х	GAA	ACUCCAUG	CAUGGAGUU UCUGUCCU
	3062	GAGGACAG	CUGAUGA :	X	GAA	AACUCCAU	AUGGAGUUU CUGUCCUC

	3063	GGAGGACA	CUGAUGA	X	GAA	AAACUCCA	UGGAGUUUC	UGUCCUCC
	3067	UUCUGGAG	CUGAUGA	X	GAA	ACAGAAAC	GUUUCUGUC	CUCCAGAA
	3070	ACUUUCUG	CUGAUGA	X	GAA	AGGACAGA	ucuguccuc	CAGAAAGU
	3083	UCCCGAUG	CUGAUGA	X	GAA	AUGCACUU	AAGUGCAUU	CAUCGGGA
5	3084	GUCCCGAU	CUGAUGA	X	GAA	AAUGCACU	AGUGCAUUC	AUCGGGAC
	3087	CAGGUCCC	CUGAUGA	X	GAA	AUGAAUGC	GCAUUCAUC	GGGACCUG
	3110	GAUAAAAG	CUGAUGA	X	GAA	AUGUUUCU	AGAAACAUC	CUUUUAUC
	3113	UCAGAUAA	CUGAUGA	Х	GAA	AGGAUGUU	AACAUCCUU	UUAUCUGA
	3114	CUCAGAUA	CUGAUGA	X	GAA	AAGGAUGU	ACAUCCUUU	UAUCUGAG
10	3115	UCUCAGAU	CUGAUGA	X	GAA	AAAGGAUG	CAUCCUUUU	AUCUGAGA
	3116	UUCUCAGA	CUGAUGA	X	GAA	AAAAGGAU	AUCCUUUUA	UCUGAGAA
	3118	UGUUCUCA	CUGAUGA	Х	GAA	AUAAAAGG	CCUUUUAUC	UGAGAACA
	3140	AAGUCGCA	CUGAUGA	х	GAA	AUCUUCAC	GUGAAGAUU	UGCGACUU
	3141	AAAGUCGC	CUGAUGA	X	GAA	AAUCUUCA	UGAAGAUUU	GCGACUUU
15	3148	CCAGGCCA	CUGAUGA	X	GAA	AGUCGCAA	UUGCGACUU	UGGCCUGG
	3149	GCCAGGCC	CUGAUGA	X	GAA	AAGUCGCA	UGCGACUUU	GGCCUGGC
	3165	CUUAUAAA	CUGAUGA	X	GAA	AUCCCGGG	CCCGGGAUA	UUUAUAAG
	3167	UUCUUAUA	CUGAUGA	X	GAA	AUAUCCCG	CGGGAUAUU	UAUAAGAA
	3168	GUUCUUAU	CUGAUGA	Х	GAA	AAUAUCCC	GGGAUAUUU	AUAAGAAC
20	316 9	GGUUCUUA	CUGAUGA	Х	GAA	AAAUAUCC	GGAUAUUUA	UAAGAACC
	3171	AGGGUUCU	CUGAUGA	X	GAA	AUAAAUAU	AUAUUUAUA	AGAACCCU
	318 3	CCUCACAU	CUGAUGA	Х	GAA	AUCAGGGU	ACCCUGAUU	AUGUG AG G
	3184	UCCUCACA	CUGAUGA	X	GAA	AAUCAGGG	CCCUGAUUA	UGUGAGGA
	3201	AAGUCGAG	CUGAUGA	Х	GAA	AUCUCCUC	GAGGAGAUA	CUCGACUU
25	3204	GGGAAGUC	CUGAUGA	X	GAA	AGUAUCUC	GAGAUACUC	GACUUCCC
	3209	UUUAGGGG	CUGAUGA	Х	GAA	AGUCGAGU	ACUCGACUU	CCCCUAAA
	3210	UUUUAGGG	CUGAUGA	X	GAA	AAGUCGAG	CUCGACUUC	CCCUAAAA
	3215	AUCCAUUU	CUGAUGA	X	GAA	AGGGGAAG	CUUCCCCUA	AAAUGGAU
	3228	GGAUUCAG	CUGAUGA	Х	GAA	AGCCAUCC	GGAUGGCUC	CUGAAUCC
30	3235	CAAAGAUG	CUGAUGA	Х	GAA	AUUCAGGA	UCCUGAAUC	CAUCUUUG
	32 39	UUGUCAAA	CUGAUGA	Х	GAA	AUGGAUUC	GAAUCCAUC	UUUGACAA
	3241	CCUUGUCA	CUGAUGA	Х	GAA	AGAUGGAU	AUCCAUCUU	UGACAAGG
	3242	ACCUUGUC	CUGAUGA	X	GAA	AAGAUGGA	UCCAUCUUU	GACAAGGU

. : : (\$

	3251	GUGCUGU	A CUGAUGA	λ >	(GA	ACCUUGUC	GACAAGGUC	UACAGCAC
	3253	UGGUGCU	G CUGAUGA	X	GA#	AGACCUUG	CAAGGUCUA	CAGCACCA
	3277	CGCCAUAC	CUGAUGA	X	GAA	ACCACACA	UGUGUGGUC	CUAUGGCG
	3280	ACACGCCA	CUGAUGA	X	GAA	AGGACCAC	GUGGUCCUA	UGGCGUGU
5	3289	CCCACAGO	CUGAUGA	X	GAA	ACACGCCA	UGGCGUGUU	GCUGUGGG
	3302	AAGGAGAA	CUGAUGA	X	GAA	AUCUCCCA	UGGGAGAUC	บบดบดดบบ
	3304	CUAAGGAG	CUGAUGA	X	GAA	AGAUCUCC	GGAGAUCUU	CUCCUUAG
	3305	CCUAAGGA	CUGAUGA	X	GAA	AAGAUCUC	GAGAUCUUC	UCCUUAGG
	3307	CCCCUAAG	CUGAUGA	X	GAA	AGAAGAUC	GAUCUUCUC	CUUAGGG
10	3310	AACCCCCU	CUGAUGA	х	GAA	AGGAGAAG	cuucuccuu	AGGGGGUU
	3311	GAACCCCC	CUGAUGA	X	GAA	AAGGAGAA	UUCUCCUUA	GGGGGUUC
	3318	GUAUGGAG	CUGAUGA	x	GAA	ACCCCCUA	UAGGGGGUU	CUCCAUAC
	3319	GGUAUGGA	CUGAUGA	x	GAA	AACCCCCU	AGGGGGUUC	UCCAUACC.
	3321	UGGGUAUG	CUGAUGA	x	GAA	AGAACCCC	GGGGUUCUC	CAUACCCA
15	332 5	CUCCUGGG	CUGAUGA	X	GAA	AUGGAGAA	UUCUCCAUA	CCCAGGAG
	3352	GGCUGCAG	CUGAUGA	x	GAA	AGUCUUCA	UGAAGACUU	CUGCAGCC
	3353	CGGCUGCA	CUGAUGA	Х	GAA	AAGUCUUC	GAAGACUUC	UGCAGCCG
	3397	GUGUGGCA	CUGAUGA	х	GAA	ACUCCGGG	CCCGGAGUA	UGCCACAC
	3413	AUUUGGUA	CUGAUGA	x	GAA	AUUUCAGG	CCUGAAAUC	UACCAAAU
20	3415	UGAUUUGG	CUGAUGA	х	GAA	AGAUUUCA	UGAAAUCUA	CCAAAUCA
	3422	UCCAACAU	CUGAUGA	х	GAA	AUUUGGUA	UACCAAAUC	AUGUUGGA
	3427	AGCAAUCC	CUGAUGA	Х	GAA	ACAUGAUU	AAUCAUGUU	GGAUUGCU
	3432	GUGCCAGC	CUGAUGA	X	GAA	AUCCAACA	UGUUGGAUU	GCUGGCAC
	3466	GUUCAGCA	CUGAUGA	Х	GAA	ACCGGGGC	GCCCCGGUU	UGCUGAAC
25	3467	AGUUCAGC	CUGAUGA	х	GAA	AACCGGGG	ccccguuu	GCUGAACU
	3476	UUCUCCAC	CUGAUGA	X	GAA	AGUUCAGC	GCUGAACUU	GUGGAGAA
	3488	AGGUCACC	CUGAUGA	X	GAA	AGUUUCUC	GAGAAACUU	GGUGACCU
	3500	UUGGCUUG	CUGAUGA	x	GAA	AGCAGGUC	GACCUGCUU	CAAGCCAA
	3501	GUUGGCUU	CUGAUGA	X	GAA	AAGCAGGU	ACCUGCUUC .	AAGCCAAC
30	3512	UCCUGUUG	CUGAUGA	x	GA'A	ACGUUGGC	GCCAACGUC	CAACAGGA
	3531	GGGGAUGU	CUGAUGA	X	GAA	AUCUUUCC	GGAAAGAUU A	ACAUCCCC
	3532	GGGGGAUG	CUGAUGA	Х	GAA	AAUCUUUC	GAAAGAUUA (CAUCCCCC
	3536	UUGAGGGG	CUGAUGA	X	GAA	AUGUAAUC	GAUUACAUC (CCCCUCAA

	3542	AUGGCAUU	CUGAUGA	X	GAA	AGGGGGAU	AUCCCCCUC	AAUGCCAU
	3551	CUAGUCAG	CUGAUGA	X	GAA	AUGGCAUU	AAUGCCAUA	CUGACUAG
	3558	ACUGUUUC	CUGAUGA	X	GAA	AGUCAGUA	UACUGACUA	GAAACAGU
	3567	UGUGAAGC	CUGAUGA	X	GAA	ACUGUUUC	GAAACAGUA	GCUUCACA
5	3571	AGUAUGUG	CUGAUGA	X	GAA	AGCUACUG	CAGUAGCUU	CACAUACU
	3572	GAGUAUGU	CUGAUGA	X	GAA	AAGCUACU	AGUAGCUUC	ACAUACUC
	3577	GGGUCGAG	CUGAUGA	Х	GAA	AUGUGAAG	CUUCACAUA	CUCGACCC
	3580	UGGGGGUC	CUGAUGA	X	GAA	AGUAUGUG	CACAUACUC	GACCCCCA
	3592	CCUCAGAG	CUGAUGA	Х	GAA	AGGUGGGG	CCCCACCUU	CUCUGAGG
10	3593	UCCUCAGA	CUGAUGA	Х	GAA	AAGGUGGG	CCCACCUUC	UCUGAGGA
	3 5 95	GGUCCUCA	CUGAUGA	Х	GAA	AGAAGGUG	CACCUUCUC	UGAGGACC
	3605	UCCUUGAA	CUGAUGA	X	GAA	AGGUCCUC	GAGGACCUU	UUCAAGGA
	3606	GUCCUUGA	CUGAUGA	х	GAA	AAGGUCCU	AGGACCUUU	UCAAGGAC
	3607	CGUCCUUG	CUGAUGA	X	GAA	AAAGGUCC	GGACCUUUU	CAAGGACG
15	3608	CCGUCCUU	CUGAUGA	X	GAA	AAAAGGUC	GACCUUUUC	AAGGACGG
	3619	GAUCUGCA	CUGAUGA	Х	GAA	AGCCGUCC	GGACGGCUU	UGCAGAUC
	3620	GGAUCUGC	CUGAUGA	Х	GAA	AAGCCGUC	GACGGCUUU	GCAGAUCC
	3627	AAAAUGUG	CUGAUGA	Х	GAA	AUCUGCAA	UUGCAGAUC	CACAUUUU
	3633	GGAAUGAA	CUGAUGA	х	GAA	AUGUGGAU	AUCCACAUU	UUCAUUCC
20	3634	CGGAAUGA	CUGAUGA	Х	GAA	AAUGUGGA	UCCACAUUU	UCAUUCCG
	3635	CCGGAAUG	CUGAUGA	Х	GAA	AAAUGUGG	CCACAUUUU	CAUUCCGG
	3636	UCCGGAAU	CUGAUGA	X	GAA	AAAAUGUG	CACAUUUUC	AUUCCGGA
	3639	GCUUCCGG	CUGAUGA	Х	GAA	AUGAAAAU	AUUUUCAUU	CCGGAAGC
	3640	AGCUUCCG	CUGAUGA	X	GAA	AAUGAAAA	UUUUCAUUC	CGGAAGCU
25	3649	CAUCAUCA	CUGAUGA	X	GAA	AGCUUCCG	CGGAAGCUC	UGAUGAUG
	3664	CGUUUACA	CUGAUGA	Х	GAA	AUCUCACA	UGUGAGAUA	UGUAAACG
	3668	AAAGCGUU	CUGAUGA	Х	GAA	ACAUAUCU	AGAUAUGUA	AACGCUUU
	3675	GAAUUUGA	CUGAUGA	Х	GAA	AGCGUUUA	UAAACGCUU	UCAAAUUC
	3676	UGAAUUUG	CUGAUGA	X	GAA	AAGCGUUU	AAACGCUUU	CAAAUUCA
30	3677	AUGAAUUU	CUGAUGA	Х	GAA	AAAGCGUU	AACGCUUUC	AAAUUCAU
	3682	GGCUCAUG	CUGAUGA	Х	GAA	AUUUGAAA	UUUCAAAUU	CAUGAGCC
	3683	AGGCUCAU	CUGAUGA	X	GAA	AAUUUGAA	UUCAAAUUC	AUGAGCCU
	3701	AAGGUUUU	CUGAUGA	Х	GAA	AUUCUUUC	GAAAGAAUC	AAAACCUU

.3

	3709	GCUCCUCA CUGAUGA X GAA AGGUUUUG	CAAAACCUU UGAGGAGC
	3710	AGCUCCUC CUGAUGA X GAA AAGGUUUU	AAAACCUUU GAGGAGCU
	3719	UUCGGUGA CUGAUGA X GAA AGCUCCUC	GAGGAGCUU UCACCGAA
	3720	GUUCGGUG CUGAUGA X GAA AAGCUCCU	AGGAGCUUU CACCGAAC
5	3721	AGUUCGGU CUGAUGA X GAA AAAGCUCC	GGAGCUUUC ACCGAACU
	3730	UGGAGGUG CUGAUGA X GAA AGUUCGGU	ACCGAACUC CACCUCCA
	3736	CAAACAUG CUGAUGA X GAA AGGUGGAG	CUCCACCUC CAUGUUUG
	3742	AGUCCUCA CUGAUGA X GAA ACAUGGAG	CUCCAUGUU UGAGGACU
	3743	UAGUCCUC CUGAUGA X GAA AACAUGGA	UCCAUGUUU GAGGACUA
10	3751	CCAGCUGA CUGAUGA X GAA AGUCCUCA	UGAGGACUA UCAGCUGG
	3753	GUCCAGCU CUGAUGA X GAA AUAGUCCU	AGGACUAUC AGCUGGAC
	3765	CAGAGUGC CUGAUGA X GAA AGUGUCCA	UGGACACUA GCACUCUG
	3 7 71	GCCCAGCA CUGAUGA X GAA AGUGCUAG	CUAGCACUC UGCUGGC
	3781	GCAAGGGG CUGAUGA X GAA AGCCCAGC	GCUGGGCUC CCCCUUGC
15	3787	GCUUCAGC CUGAUGA X GAA AGGGGGAG	CUCCCCCUU GCUGAAGC
	3799	UCCAGGUG CUGAUGA X GAA ACCGCUUC	GAAGCGGUU CACCUGGA
	3800	GUCCAGGU CUGAUGA X GAA AACCGCUU	AAGCGGUUC ACCUGGAC
	3829	UCUUCAUG CUGAUGA X GAA AGGCCUUG	CAAGGCCUC CAUGAAGA
	3839	CUCAAGUC CUGAUGA X GAA AUCUUCAU	AUGAAGAUA GACUUGAG
20	3844	CUAUUCUC CUGAUGA X GAA AGUCUAUC	GAUAGACUU GAGAAUAG
	3851	UUACUCGC CUGAUGA X GAA AUUCUCAA	UUGAGAAUA GCGAGUAA
	3858	CUUGCUUU CUGAUGA X GAA ACUCGCUA	UAGCGAGUA AAAGCAAG
	3 8 78	AGAUCGGA CUGAUGA X GAA AGUCCCGC	GCGGGACUU UCCGAUCU
	3879	CAGAUCGG CUGAUGA X GAA AAGUCCCG	CGGGACUUU CCGAUCUG
25	3880	GCAGAUCG CUGAUGA X GAA AAAGUCCC	GGGACUUUC CGAUCUGC
	3885	CCUCGGCA CUGAUGA X GAA AUCGGAAA	UUUCCGAUC UGCCGAGG
	3901	AGAAGCAG CUGAUGA X GAA AGCUGGGC	GCCCAGCUU CUGCUUCU
	3902	GAGAAGCA CUGAUGA X GAA AAGCUGGG	CCCAGCUUC UGCUUCUC
	3907	AGCUGGAG CUGAUGA X GAA AGCAGAAG	CUUCUGCUU CUCCAGCU
30	3908	CAGCUGGA CUGAUGA X GAA AAGCAGAA	UUCUGCUUC UCCAGCUG
	3910	CACAGCUG CUGAUGA X GAA AGAAGCAG	CUGCUUCUC CAGCUGUG
	3926	ACGGGCCU CUGAUGA X GAA AUGUGGCC	GGCCACAUC AGGCCCGU
	3949	CCAGCUCA CUGAUGA X GAA AUUCAUCG	CGAUGAAUC UGAGCUGG

	3967	AACAGCAG	CUGAUGA	X	GAA	ACUCCUUU	AAAGGAGUC	CUGCUGUU
	3975	GGGUGGAG	CUGAUGA	х	GAA	ACAGCAGG	CCUGCUGUU	CUCCACCC
	3976	GGGGUGGA	CUGAUGA	X	GAA	AACAGCAG	CUGCUGUUC	UCCACCCC
	3978	UGGGGGUG	CUGAUGA	X	GAA	AGAACAGC	GCUGUUCUC	CACCCCCA
5	3991	CGGAGUUG	CUGAUGA	X	GAA	AGUCUGGG	CCCAGACUA	CAACUCCG
	3 9 97	ACACCACG	CUGAUGA	X	GAA	AGUUGUAG	CUACAACUC	CGUGGUGU
	4006	AGGAGUAC	CUGAUGA	Х	GAA	ACACCACG	CGUGGUGUU	GUACUCCU
	4009	GGGAGGAG	CUGAUGA	Х	GAA	ACAACACC	GGUGUUGUA	CUCCUCCC
	4012	GCGGGGAG	CUGAUGA	Х	GAA	AGUACAAC	GUUGUACUC	CUCCCCGC
10	4015	CGGGCGGG	CUGAUGA	Х	GAA	AGGAGUAC	GUACUCCUC	CCCGCCCG
	4027	AGAAGCUU	CUGAUGA	X	GAA	AGGCGGGC	GCCCGCCUA	AAGCUUCU
	4033	CUGGUGAG	CUGAUGA	X	GAA	AGCUUUAG	CUAAAGCUU	CUCACCAG
	4034	GCUGGUGA	CUGAUGA	Х	GAA	AAGCUUUA	UAAAGCUUC	UCACCAGC
	4036	GGGCUGGU	CUGAUGA	X	GAA	AGAAGCUU	AAGCUUCUC	ACCAGCCC
15	4066	AUGUAUAA	CUGAUGA	Х	GAA	ACUGUCAG	CUGACAGUA	UUAUACAU
	4068	AGAUGUAU	CUGAUGA	Х	GAA	AUACUGUC	GACAGUAUU	AUACAUCU
	4069	UAGAUGUA	CUGAUGA	Х	GAA	AAUACUGU	ACAGUAUUA	UACAUCUA
	4071	CAUAGAUG	CUGAUGA	X	GAA	AUAAUACU	AGUAUUAUA	CAUCUAUG
	4075	AACUCAUA	CUGAUGA	Х	GAA	AUGUAUAA	UUAUACAUÇ	UAUGAGUU
20	4077	UAAACUCA	CUGAUGA	X	GAA	AGAUGUAU	AUACAUCUA	UGAGUUUA
	4083	UAGGUGUA	CUGAUGA	Х	GAA	ACUCAUAG	CUAUGAGUU	UACACCUA
	4084	AUAGGUGU	CUGAUGA	Х	GAA	AACUCAUA	UAUGAGUUU	ACACCUAU
	4085	AAUAGGUG	CUGAUGA	Х	GAA	AAACUCAU	AUGAGUUUA	CACCUAUU
	4091	GAGCGGAA	CUGAUGA	Х	GAA	AGGUGUAA	UUACACCUA	UUCCGCUC
25	4093	UGGAGCGG	CUGAUGA	X	GAA	AUAGGUGU	ACACCUAUU	CCGCUCCA
	4094	GUGGAGCG	CUGAUGA	X	GAA	AAUAGGUG	CACCUAUUC	CGCUCCAC
	4099	CUCCUGUG	CUGAUGA	Х	GAA	AGCGGAAU	AUUCCGCUC	CACAGGAG
	4117	GUCACGAA	CUGAUGA	Х	GAA	AGCAGCUG	CAGCUGCUU	UUCGUGAC
	4118	GGUCACGA	CUGAUGA	Х	GAA	AAGCAGCU	AGCUGCUUU	UCGUGACC
30	4119	AGGUCACG	CUGAUGA	Х	GAA	AAAGCAGC	GCUGCUUUU	CGUGACCU
	4120					AAAAGCAG	CUGCUUUUC	GUGACCUU
	4128					AGGUCACG	CGUGACCUU	UAAUCGUG
	4129	GCACGAUU	CUGAUGA	X	GAA	AAGGUCAC	GUGACCUUU	AAUCGUGC

	4130	AGCACGAU CUGAUGA X GAA AAAGGUCA	UGACCUUUA AUCGUGCU
	4133	AAAAGCAC CUGAUGA X GAA AUUAAAGG	CCUUUAAUC GUGCUUUU
	4139	AAACAAAA CUGAUGA X GAA AGCACGAU	AUCGUGCUU UUUUGUUU
	4140	AAAACAAA CUGAUGA X GAA AAGCACGA	บCGUGCUUU บบบGUUUU
5	4141	AAAAACAA CUGAUGA X GAA AAAGCACG	cgugcuuuu uuguuuuu
	4142	AAAAAACA CUGAUGA X GAA AAAAGCAC	gugcuuuuu uguuuuuu
	4143	CAAAAAC CUGAUGA X GAA AAAAAGCA	UGCUUUUUU GUUUUUUG
	4146	AAACAAAA CUGAUGA X GAA ACAAAAA	บบบบบบเรียบ บบบบเรียบบ
	4147	AAAACAAA CUGAUGA X GAA AACAAAAA	บบบบนเริ่มบน บบบเริ่มบบบ
10	4148	CAAAACAA CUGAUGA X GAA AAACAAAA	บบบบเรียบบบ บบเรียบบบเร
	4149	ACAAAACA CUGAUGA X GAA AAAACAAA	บบบดบบบบบ บดบบบบดบ
	4150	AACAAAAC CUGAUGA X GAA AAAAACAA	บบดบบบบบบ ดบบบบดบบ ่
	4153	ACAAACAA CUGAUGA X GAA ACAAAAA	บบบบบบเดินก การการการการการการการการการการการการการก
	4154	AACAAACA CUGAUGA X GAA AACAAAAA	บบบบบเริ่มบบ บเริ่มบบเริ่มบ
15	4155	CAACAAAC CUGAUGA X GAA AAACAAAA	บบบบเรียบบบ เรียบบเรียบเร
	4158	CAACAACA CUGAUGA X GAA ACAAAACA	UGUUUUGUU UGUUGUUG
	4159	GCAACAAC CUGAUGA X GAA AACAAAAC	GUUUUGUUU GUUGUUGC
	4162	ACAGCAAC CUGAUGA X GAA ACAAACAA	UUGUUUGUU GUUGCUGU
	4165	AAAACAGC CUGAUGA X GAA ACAACAAA	บบบเรบบเรบบ เรียบบบบ
20	4171	UUAGUCAA CUGAUGA X GAA ACAGCAAC	GUUGCUGUU UUGACUAA
	4172	GUUAGUCA CUGAUGA X GAA AACAGCAA	UUGCUGUUU UGACUAAC
	4173	UGUUAGUC CUGAUGA X GAA AAACAGCA	UGCUGUUUU GACUAACA
	4178	AUUCUUGU CUGAUGA X GAA AGUCAAAA	UUUUGACUA ACAAGAAU
	4189	ACUGGGGU CUGAUGA X GAA ACAUUCUU	AAGAAUGUA ACCCCAGU
25	4198	ACGUCACU CUGAUGA X GAA ACUGGGGU	
	4199	CACGUCAC CUGAUGA X GAA AACUGGGG	
	4216	AACAAUAG CUGAUGA X GAA AUUCUUCA	
	4219	UCUAACAA CUGAUGA X GAA AGUAUUCU	
	4221	UCUCUAAC CUGAUGA X GAA AUAGUAUU	AAUACUAUU GUUAGAGA
30	4224		ACUAUUGUU AGAGAAAU
	4225	GAUUUCUC CUGAUGA X GAA AACAAUAG	
	4233	GCGGGGG CUGAUGA X GAA AUUUCUCU	
	4249	GUUACCCU CUGAUGA X GAA AGGCUUUG	CAAAGCCIIC AGCCIIAAG

	4255	GUCCAGGU	CUGAUGA	X	GAA	ACCCUGAG	CUCAGGGUA	ACCUGGAC
	4282	GGUCGCCA	CUGAUGA	Х	GAA	AGGCACCU	AGGUGCCUC	UGGCGACC
	4323	GCUGCAGG	CUGAUGA	Х	GAA	AGGGUGGG	CCCACCCUC	CCUGCAGC
	4341	ACUGCCUC	CUGAUGA	X	GAA	AGUCCCAC	GUGGGACUA	GAGGCAGU
5	4350	AAUGGGCU	CUGAUGA	Х	GAA	ACUGCCUC	GAGGCAGUA	AGCCCAUU
	4358	CAUGAGCU	CUGAUGA	X	GAA	AUGGGCUU	AAGCCCAUU	AGCUCAUG
	4359	CCAUGAGC	CUGAUGA	X	GAA	AAUGGGCU	AGCCCAUUA	GCUCAUGG
	4363	GCAGCCAU	CUGAUGA	Х	GAA	AGCUAAUG	CAUUAGCUC	AUGGCUGC
	4387	GAGAGACA	CUGAUGA	X	GAA	AGCAGGUC	GACCUGCUC	UGUCUCUC
10	4391	AUAAGAGA	CUGAUGA	Х	GAA	ACAGAGCA	UGCUCUGUC	UCUCUUAU
	4393	CCAUAAGA	CUGAUGA	Х	GAA	AGACAGAG	CUCUGUCUC	UCUUAUGG
	4395	CUCCAUAA	CUGAUGA	X	GAA	AGAGACAG	CUGUCUCUC	UUAUGGAG
	4397	UCCUCCAU	CUGAUGA	X	GAA	AGAGAGAC	GUCUCUCUU	AUGGAGGA
	4398	UUCCUCCA	CUGAUGA	Х	GAA	AAGAGAGA	UCUCUCUUA	UGGAGGAA
15	4445	GCAUCCCA	CUGAUGA	Х	GAA	AGCCUUUU	AAAAGGCUU	UGGGAUGC
	4446	CGCAUCCC	CUGAUGA	Х	GAA	AAGCCUUU	AAAGGCUUU	GGGAUGCG
	4456	ACAGGACG	CUGAUGA	Х	GAA	ACGCAUCC	GGAUGCGUC	CGUCCUGU
	4460	CUCCACAG	CUGAUGA	Х	GAA	ACGGACGC	GCGUCCGUC	CUGUGGAG
	4487	GCAUAGCG	CUGAUGA	X	GAA	AGCCCCCU	AGGGGCUC	CGCUAUGC
20	4492	AAGUGGCA	CUGAUGA	X	GAA	AGCGGAGC	GCUCCGCUA	UGCCACUU
	4500	AGUCACUG	CUGAUGA	Х	GAA	AGUGGCAU	AUGCCACUU	CAGUGACU
	4501	AAGUCACU	CUGAUGA	X	GAA	AAGUGGCA	UGCCACUUC	AGUGACUU
	4509	GGAGUGAG	CUGAUGA	Х	GAA	AGUCACUG	CAGUGACUU	CUCACUCC
	4510	AGGAGUGA	CUGAUGA	Х	GAA	AAGUCACU	AGUGACUUC	UCACUCCU
25	4512	CCAGGAGU	CUGAUGA	X	GAA	AGAAGUCA	UGACUUCUC	ACUCCUGG
	4516	GAGGCCAG	CUGAUGA	X	GAA	AGUGAGAA	UUCUCACUC	CUGGCCUC
	4524	AAACAGCG	CUGAUGA	X	GAA	AGGCCAGG	CCUGGCCUC	CGCUGUUU
	4531	GGGCCCGA	CUGAUGA	X	GAA	ACAGCGGA	UCCGCUGUU	UCGGGCCC
	4532	GGGGCCCG	CUGAUGA	X	GAA	AACAGCGG	CCGCUGUUU	CGGGCCCC
30	4533	GGGGGCCC	CUGAUGA	X	GAA	AAACAGCG	CGCUGUUUC	GGGCCCCC
	4543	CCUCUUGG	CUGAUGA	Х	GAA	AGGGGGCC	GGCCCCCUU	CCAAGAGG
	4544	ACCUCUUG	CUGAUGA	X	GAA	AAGGGGGC	GCCCCCUUC	CAAGAGGU
	455 3	UGCUCUGA	CUGAUGA	X	GAA	ACCUCUUG	CAAGAGGUA	UCAGAGCA

2.5

f.t set to

	4555	UCUGCUCU CUGAUGA X GAA AUACCUCU	AGAGGUAUC AGAGCAGA
	4577	GUCUAGGA CUGAUGA X GAA ACGUCCCU	AGGGACGUU UCCUAGAC
	4578	GGUCUAGG CUGAUGA X GAA AACGUCCC	GGGACGUUU CCUAGACC
	4579	UGGUCUAG CUGAUGA X GAA AAACGUCC	GGACGUUUC CUAGACCA
5	4582	CCCUGGUC CUGAUGA X GAA AGGAAACG	CGUUUCCUA GACCAGGG
	4598	UUCCCGAG CUGAUGA X GAA ACAUGUGC	GCACAUGUU CUCGGGAA
	459 9	GUUCCCGA CUGAUGA X GAA AACAUGUG	CACAUGUUC UCGGGAAC
	4601	UGGUUCCC CUGAUGA X GAA AGAACAUG	CAUGUUCUC GGGAACCA
	4614	UUAAGAUU CUGAUGA X GAA ACUGUGGU	ACCACAGUU AAUCUUAA
10	461 5	UUUAAGAU CUGAUGA X GAA AACUGUGG	CCACAGUUA AUCUUAAA
	4618	AGAUUUAA CUGAUGA X GAA AUUAACUG	CAGUUAAUC UUAAAUCU
	4620	AAAGAUUU CUGAUGA X GAA AGAUUAAC	GUUAAUCUU AAAUCUUU
	4621	AAAAGAUU CUGAUGA X GAA AAGAUUAA	UUAAUCUUA AAUCUUUU
	4625	CGGGAAAA CUGAUGA X GAA AUUUAAGA	UCUUAAAUC UUUUCCCG
15	4627	CCCGGGAA CUGAUGA X GAA AGAUUUAA	UUAAAUCUU UUCCCGGG
	4628	UCCCGGGA CUGAUGA X GAA AAGAUUUA	UAAAUCUUU UCCCGGGA
	4629	CUCCCGGG CUGAUGA X GAA AAAGAUUU	AAAUCUUUU CCCGGGAG
	4630	ACUCCCGG CUGAUGA X GAA AAAAGAUU	AAUCUUUUC CCGGGAGU
	4639	CAACAGAA CUGAUGA X GAA ACUCCCGG	CCGGGAGUC UUCUGUUG
20	4641	GACAACAG CUGAUGA X GAA AGACUCCC	GGGAGUCUU CUGUUGUC
	4642	AGACAACA CUGAUGA X GAA AAGACUCC	GGAGUCUUC UGUUGUCU
	4646	AAACAGAC CUGAUGA X GAA ACAGAAGA	UCUUCUGUU GUCUGUUU
	4649	GGUAAACA CUGAUGA X GAA ACAACAGA	UCUGUUGUC UGUUUACC
	4653	GGAUGGUA CUGAUGA X GAA ACAGACAA	UUGUCUGUU UACCAUCC
25	4654	UGGAUGGU CUGAUGA X GAA AACAGACA	UGUCUGUUU ACCAUCCA
	4655	UUGGAUGG CUGAUGA X GAA AAACAGAC	00.1000.11
	4660	AUGCUUUG CUGAUGA X GAA AUGGUAAA	
	46 69	AUGUUAAA CUGAUGA X GAA AUGCUUUG	CAAAGCAUA UUUAACAU
2.0	4671	ACAUGUUA CUGAUGA X GAA AUAUGCUU	AAGCAUAUU UAACAUGU
30	4672	CACAUGUU CUGAUGA X GAA AAUAUGCU	AGCAUAUUU AACAUGUG
	4673	ACACAUGU CUGAUGA X GAA AAAUAUGC	GCAUAUUUA ACAUGUGU
	4682	CCCCCACU CUGAUGA X GAA ACACAUGU	ACAUGUGUC AGUGGGG
	4698	CAGAAGCC CUGAUGA X GAA AGCGCCAC	GUGGCGCUU GGCUUCUG

	4703	GGCCUCAG	CUGAUGA	Х	GAA	AGCCAAGC	GCWGGCW	CUGAGGCC
	4704	UGGCCUCA	CUGAUGA	х	GAA	AAGCCAAG	CUUGGCUUC	UGAGGCCA
	4720	GAACUGAU	CUGAUGA	X	GAA	AUGGCUCU	AGAGCCAUC	AUCAGUUC
	4723	GAGGAACU	CUGAUGA	x	GAA	AUGAUGGC	GCCAUCAUC	AGUUCCUC
5	47 27	ACUAGAGG	CUGAUGA	X	GAA	ACUGAUGA	UCAUCAGUU	CCUCUAGU
	4728	CACUAGAG	CUGAUGA	x	GAA	AACUGAUG	CAUCAGUUC	CUCUAGUG
	4731	UCUCACUA	CUGAUGA	x	GAA	AGGAACUG	CAGUUCCUC	UAGUGAGA
	4733	CAUCUCAC	CUGAUGA	x	GAA	AGAGGAAC	GUUCCUCUA	GUGAGAUG
	4745	AUGACCUC	CUGAUGA	Х	GAA	AUGCAUCU	AGAUGCAUU	GAGGUCAU
10	4751	UUGGGUAU	CUGAUGA	Х	GAA	ACCUCAAU	AUUGAGGUC	AUACCCAA
	4754	AGCUUGGG	CUGAUGA	X	GAA	AUGACCUC	GAGGUCAUA	CCCAAGCU
	476 3	AGGCCUGC	CUGAUGA	Х	GAA	AGCUUGGG	CCCAAGCUU	GCAGGCCU
	4777	AGUAUGCG	CUGAUGA	x	GAA	AGGUCAGG	CCUGACCUU	CGCAUACU
	47 78	CAGUAUGC	CUGAUGA	Х	GAA	AAGGUCAG	CUGACCUUC	GCAUACUG
15	4783	GUGAGCAG	CUGAUGA	X	GAA	AUGCGAAG	CUUCGCAUA	CUGCUCAC
	478 9	CUCCCCGU	CUGAUGA	х	GAA	AGCAGUAU	AUACUGCUC	ACGGGGAG
	4799	GACCACUU	CUGAUGA	Х	GAA	ACUCCCCG	CGGGGAGUU	AAGUGGUC
	4800	GGACCACU	CUGAUGA	Х	GAA	AACUCCCC	GGGGAGUUA	AGUGGUCC
	4807	CCAAACUG	CUGAUGA	x	GAA	ACCACUUA	UAAGUGGUC	CAGUUUGG
20	4812	CUAGGCCA	CUGAUGA	Х	GAA	ACUGGACC	GGUCCAGUU	UGGCCUAG
	4813	ACUAGGCC	CUGAUGA	$\mathbf{x}_{_{_{\mathbf{x}}}}$	GAA	AACUGGAC	GUCCAGUUU	GGCCUAGU
	4819	AACCUUAC	CUGAUGA	Х	GAA	AGGCCAAA	UUUGGCCUA	GUAAGGUU
	4822	GGCAACCU	CUGAUGA	X	GAA	ACUAGGCC	GGCCUAGUA	AGGUUGCC
	4827	CAGUAGGC	CUGAUGA	Х	GAA	ACCUUACU	AGUAAGGUU	GCCUACUG
2 5	4832	CCCAUCAG	CUGAUGA	Х	GAA	AGGCAACC	GGUUGCCUA	CUGAUGGG
	484 3	UGGCUUUU	CUGAUGA	X,	GAA	AGCCCAUC	GAUGGGCUC	AAAAGCCA
	4855	CUGUUUAA	CUGAUGA	Х	GAA	AUGUGGCU	AGCCACAUU	UUAAACAG
	4856	CCUGUUUA	CUGAUGA	X	GAA	AAUGUGGC	GCCACAUUU	UAAACAGG
	48 57	ACCUGUUU	CUGAUGA	Х	GAA	AAAUGUGG	CCACAUUUU	AAACAGGU
30	4858	AACCUGUU	CUGAUGA	Х	GAA	AAAAUGUG	CACAUUUUA	AACAGGUU
	48 66	UGAGAUAA	CUGAUGA	X	GAA	ACCUGUUU	AAACAGGUU	UUAUCUCA
	4867	UUGAGAUA	CUGAUGA	X	GAA	AACCUGUU	AACAGGUUU	UAUCUCAA
	4868	CUUGAGAU	CUGAUGA	Х	GAA	AAACCUGU	ACAGGUUUU	AUCUCAAG

	4869	9 ACUUGAGA CUGAUGA X GAA AAAACCUG	CAGGUUUUA UCUCAAGU
	4871	AUACUUGA CUGAUGA X GAA AUAAAACC	GGUUUUAUC UCAAGUAU
	4873	B UAAUACUU CUGAUGA X GAA AGAUAAAA	UUUUAUCUC AAGUAUUA
	4878	B UAUAUUAA CUGAUGA X GAA ACUUGAGA	UCUCAAGUA UUAAUAUA
5	4880	UAUAUAUU CUGAUGA X GAA AUACUUGA	UCAAGUAUU AAUAUAUA
	4881	CUAUAUAU CUGAUGA X GAA AAUACUUG	CAAGUAUUA AUAUAUAG
	4884	UGUCUAUA CUGAUGA X GAA AUUAAUAC	GUAUUAAUA UAUAGACA
	4886	CUUGUCUA CUGAUGA X GAA AUAUUAAU	AUUAAUAUA UAGACAAG
	488 8	GUCUUGUC CUGAUGA X GAA AUAUAUUA	UAAUAUAUA GACAAGAC
10	4900	UAAUGCAU CUGAUGA X GAA AGUGUCUU	AAGACACUU AUGCAUUA
	4901	AUAAUGCA CUGAUGA X GAA AAGUGUCU	AGACACUUA UGCAUUAU
	4907	AACAGGAU CUGAUGA X GAA AUGCAUAA	UUAUGCAUU AUCCUGUU
	4908	AAACAGGA CUGAUGA X GAA AAUGCAUA	
	4910	STATE COURTOR & GAR AUAAUGCA	UGCAUUAUC CUGUUUUA
15	4915	AUAUAUAA CUGAUGA X GAA ACAGGAUA	UAUCCUGUU UUAUAUAU
	4916	GAUAUAUA CUGAUGA X GAA AACAGGAU	AUCCUGUUU UAUAUAUC
	4917	GGAUAUAU CUGAUGA X GAA AAACAGGA	UCCUGUUUU AUAUAUCC
	4918	UGGAUAUA CUGAUGA X GAA AAAACAGG	CCUGUUUUA UAUAUCCA
	4920	AUUGGAUA CUGAUGA X GAA AUAAAACA	UGUUUUAUA UAUCCAAU
20	4922	UCAUUGGA CUGAUGA X GAA AUAUAAAA	UUUUAUAUA UCCAAUGA
	4924	AUUCAUUG CUGAUGA X GAA AUAUAUAA	0.1100,110
	4933	CCCAGUUA CUGAUGA X GAA AUUCAUUG	CAAUGAAUA UAACUGGG
	4935	GCCCCAGU CUGAUGA X GAA AUAUUCAU	AUGAAUAUA ACUGGGGC
	4948	UGACUCUU CUGAUGA X GAA ACUCGCCC	GGGCGAGUU AAGAGUCA
25	4949	AUGACUCU CUGAUGA X GAA AACUCGCC	GGCGAGUUA AGAGUCAU
	4955	UAGACCAU CUGAUGA X GAA ACUCUUAA	UUAAGAGUC AUGGUCUA
	4961	CUUUUCUA CUGAUGA X GAA ACCAUGAC	GUCAUGGUC UAGAAAAG
	4963	CCCUUUUC CUGAUGA X GAA AGACCAUG	CAUGGUCUA GAAAAGGG
	4974	UACAGAGA CUGAUGA X GAA ACCCCUUU	AAAGGGGUU UCUCUGUA
30	4975	GUACAGAG CUGAUGA X GAA AACCCCUU	AAGGGGUUU CUCUGUAC
	4976	GGUACAGA CUGAUGA X GAA AAACCCCU	AGGGGUUUC UCUGUACC
	4978	UGGGUACA CUGAUGA X GAA AGAAACCC	GGGUUUCUC UGUACCCA
	4982	GAUUUGGG CUGAUGA X GAA ACAGAGAA	UUCUCUGUA CCCAAAUC

PCT/US96/17480

	4990	ACCAGCCC	CUGAUGA	X	GAA	AUUUGGGU	ACCCAAAUC	GGGCUGGU
	49 99	CUUGGUCC	CUGAUGA	х	GAA	ACCAGCCC	GGGCUGGUU	GGACCAAG
	5029	GCUGGGAC	CUGAUGA	Х	GAA	ACCACUCU	AGAGUGGUU	GUCCCAGC
	5032	AUAGCUGG	CUGAUGA	X	GAA	ACAACCAC	GUGGUUGUC	CCAGCUAU
5	50 39	AGUAACUA	CUGAUGA	X	GAA	AGCUGGGA	UCCCAGCUA	UAGUUACU
	5041	UUAGUAAC	CUGAUGA	X	GAA	AUAGCUGG	CCAGCUAUA	GUUACUAA
	5044	AGUUUAGU	CUGAUGA	х	GAA	ACUAUAGC	GCUAUAGUU	ACUAAACU
	5045	UAGUUUAG	CUGAUGA	Х	GAA	AACUAUAG	CUAUAGUUA	CUAAACUA
	5048	GAGUAGUU	CUGAUGA	Х	GAA	AGUAACUA	UAGUUACUA	AACUACUC
10	505 3	UGGGUGAG	CUGAUGA	Х	GAA	AGUUUAGU	ACUAAACUA	CUCACCCA
	5056	CUUUGGGU	CUGAUGA	Х	GAA	AGUAGUUU	AAACUACUC	ACCCAAAG
	5066	GAGGUCCC	CUGAUGA	Х	GAA	ACUUUGGG	CCCAAAGUU	GGGACCUC
	5074	AAGCCAGU	CUGAUGA	х	GAA	AGGUCCCA	UGGGACCUC	ACUGGCUU
	5082	GUAAAGAG	CUGAUGA	Х	GAA	AGCCAGUG	CACUGGCUU	CUCUUUAC
15	508 3	AGUAAAGA	CUGAUGA	Х	GAA	AAGCCAGU	ACUGGCUUC	UCUUUACU
	5085	GAAGUAAA	CUGAUGA	x	GAA	AGAAGCCA	UGGCUUCUC	UUUACUUC
	5087	AUGAAGUA	CUGAUGA	Х	GAA	AGAGAAGC	GCUUCUCUU	UACUUCAU
	5088	GAUGAAGU	CUGAUGA	X	GAA	AAGAGAAG	CUUCUCUUU	ACUUCAUC
	508 9	UGAUGAAG	CUGAUGA	Х	GAA	AAAGAGAA	UUCUCUUUA	CUUCAUCA
20	5092	CCAUGAUG	CUGAUGA	X	GAA	AGU AAAG A	UCUUUACUU	CAUCAUGG
	509 3	UCCAUGAU	CUGAUGA	Х	GAA	AAGU AAA G	CUUUACUUC	AUCAUGGA
	509 6	AAAUCCAU	CUGAUGA	х	GAA	AUGAAGUA	UACUUCAUC	AUGGAUUU
	5103	GAUGGUGA	CUGAUGA	X	GAA	AUCCAUGA	UCAUGGAUU	UCACCAUC
	5104	GGAUGGUG	CUGAUGA	Х	GAA	AAUCCAUG	CAUGGAUUU	CACCAUCC
25	51 05	GGGAUGGU	CUGAUGA	Х	GAA	AAAUCCAU	AUGGAUUUC	ACCAUCCC
	5111	UGCCUUGG	CUGAUGA	Х	GAA	AUGGUGAA	UUCACCAUC	CCAAGGCA
	5122	UCCUCUCA	CUGAUGA	Х	GAA	ACUGCCUU	AAGGCAGUC	UGAGAGGA
	5134	AUACUCUU	CUGAUGA	X	GAA	AGCUCCUC	GAGGAGCUA	AAGAGUAU
	5141	UGGGCUGA	CUGAUGA	Х	GAA	ACUCUUUA	UAAAGAGUA	UCAGCCCA
30	5143	UAUGGGCU	CUGAUGA	Х	GAA	AUACUCUU	AAGAGUAUC	AGCCCAUA
	5151	UUAAUAAA	CUGAUGA	X	GAA	AUGGGCUG	CAGCCCAUA	AAUUAUUU
	51 53	GCUUAAUA	CUGAUGA	Х	GAA	AUAUGGC	GCCCAUAUU	UAUUAAGC
	5154	UGCUUAAU	CUGAUGA	X	GAA	AAUAUG GG	CCCAUAUUU	AUUAAGCA

	5155	GUGCUUAA CUGAUGA X GAA AAAUAUGG	CCAUAUUUA UUAAGCAC
	5157	AAGUGCUU CUGAUGA X GAA AUAAAUAU	AUAUUUAUU AAGCACUU
	5158	AAAGUGCU CUGAUGA X GAA AAUAAAUA	UAUUUAUUA AGCACUUU
	516 5	GGAGCAUA CUGAUGA X GAA AGUGCUUA	UAAGCACUU UAUGCUCC
5	516 6	AGGAGCAU CUGAUGA X GAA AAGUGCUU	AAGCACUUU AUGCUCCU
	5167	AAGGAGCA CUGAUGA X GAA AAAGUGCU	AGCACUUUA UGCUCCUU
	5172	GUGCCAAG CUGAUGA X GAA AGCAUAAA	UUUAUGCUC CUUGGCAC
	5175	GCUGUGCC CUGAUGA X GAA AGGAGCAU	AUGCUCCUU GGCACAGC
	5195	GCAUAAAU CUGAUGA X GAA ACACAUCA	UGAUGUGUA AUUUAUGC
10	5198	CUUGCAUA CUGAUGA X GAA AUUACACA	UGUGUAAUU UAUGCAAG
•	5199	GCUUGCAU CUGAUGA X GAA AAUUACAC	GUGUAAUUU AUGCAAGC
	5200	AGCUUGCA CUGAUGA X GAA AAAUUACA	UGUAAUUUA UGCAAGCU
	5209	UGGAGAGG CUGAUGA X GAA AGCUUGCA	UGCAAGCUC CCUCUCCA
	521 3	UAGCUGGA CUGAUGA X GAA AGGGAGCU	AGCUCCCUC UCCAGCUA
15	521 5	CCUAGCUG CUGAUGA X GAA AGAGGGAG	CUCCCUCUC CAGCUAGG
	5221	CUGAGUCC CUGAUGA X GAA AGCUGGAG	CUCCAGCUA GGACUCAG
	5227	AAUAUCCU CUGAUGA X GAA AGUCCUAG	CUAGGACUC AGGAUAUU
	523 3	UUGACUAA CUGAUGA X GAA AUCCUGAG	CUCAGGAUA UUAGUCAA
	523 5	CAUUGACU CUGAUGA X GAA AUAUCCUG	CAGGAUAUU AGUCAAUG
20	5236	UCAUUGAC CUGAUGA X GAA AAUAUCCU	AGGAUAUUA GUCAAUGA
	5239	GGCUCAUU CUGAUGA X GAA ACUAAUAU	AUAUUAGUC AAUGAGCC
	5250	UUCCUUUU CUGAUGA X GAA AUGGCUCA	UGAGCCAUC AAAAGGAA
	5273	AAAUAAGA CUGAUGA X GAA AGGUUUUU	AAAAACCUA UCUUAUUU
	5275	GAAAAUAA CUGAUGA X GAA AUAGGUUU	AAACCUAUC UUAUUUUC
25	5277	AUGAAAAU CUGAUGA X GAA AGAUAGGU	
	52 78	GAUGAAAA CUGAUGA X GAA AAGAUAGG	
	5280	CAGAUGAA CUGAUGA X GAA AUAAGAUA	
	5281	ACAGAUGA CUGAUGA X GAA AAUAAGAU	
	5282	AACAGAUG CUGAUGA X GAA AAAUAAGA	41.00000
30	5283	AAACAGAU CUGAUGA X GAA AAAAUAAG	
	5286	AUGAAACA CUGAUGA X GAA AUGAAAAU	20000010
	5290	AGGUAUGA CUGAUGA X GAA ACAGAUGA	UCAUCUGUU UCAUACCU
	5291	AAGGUAUG CUGAUGA X GAA AACAGAUG	CAUCUGUUU CAUACCUU

PCT/US96/17480

	5 29 2	CAAGGUAU	CUGAUGA	х	GAA	AAACAGAU	AUCUGUUUC	AUACCUUG
	529 5	AGACAAGG	CUGAUGA	х	GAA	AUGAAACA	UGUUUCAUA	ccuugucu
	5299	CCCCAGAC	CUGAUGA	Х	GAA	AGGUAUGA	UCAUACCUU	GUCUGGGG
	530 2	AGACCCCA	CUGAUGA	Х	GAA	ACAAGGUA	UACCUUGUC	UGGGGUCU
5	5309	CGUCAUUA	CUGAUGA	х	GAA	ACCCCAGA	UCUGGGGUC	UAAUGACG
	5311	AUCGUCAU	CUGAUGA	х	GAA	AGACCCCA	UGGGGUCUA	AUGACGAU
	5331	CCCAUGUC	CUGAUGA	х	GAA	ACCCUGUU	AACAGGGUA	GACAUGGG
	5350	CCCUUUUC	CUGAUGA	X	GAA	ACCCUGUC	GACAGGGUA	GAAAAGGG
	5367	.ACCCCAAA	CUGAUGA	x	GAA	AGCGGGCA	UGCCCGCUC	UUUGGGGU
10	536 9	AGACCCCA	CUGAUGA	Х	GAA	AGAGCGGG	CCCGCUCUU	UGGGGUCU
	537 0	UAGACCCC	CUGAUGA	X	GAA	AAGAGCGG	CCGCUCUUU	GGGGUCUA
	5376	CAUCUCUA	CUGAUGA	X	GAA	ACCCCAAA	UUUGGGGUC	UAGAGAUG
	5378	CUCAUCUC	CUGAUGA	х	GAA	AGACCCCA	UGGGGUCUA	GAGAUGAG
	5395	AUUUUAGA	CUGAUGA	X	GAA	ACCCAGGG	CCCUGGGUC	UCUAAAAU
15	5397	CCAUUUUA	CUGAUGA	Х	GAA	AGACCCAG	CUGGGUCUC	UAAAAUGG
	5 39 9	AGCCAUUU	CUGAUGA	Х	GAA	AGAGACCC	GGGUCUCUA	AAAUGGCU
	5408	UUCUAAGA	CUGAUGA	Х	GAA	AGCCAUUU	AAAUGGCUC	UCUUAGAA
	5410	ACUUCUAA	CUGAUGA	Х	GAA	AGAGCCAU	AUGGCUCUC	UUAGAAGU
	5412	CAACUUCU	CUGAUGA	Х	GAA	AGAGAGCC	GGCUCUCUU	AGAAGUUG
20	5413	ACAACUUC	CUGAUGA	Х	GAA	AAGAGAGC	GCUCUCUUA	GAAGUUGU
	5419	GCACAUAC	CUGAUGA	Х	GAA	ACUUCUAA	UUAGAAGUU	GUAUGUGC
	5422	UUUGCACA	CUGAUGA	X	GAA	ACAACUUC	GAAGUUGUA	UGUGCAAA
	5432	CAGACCAU	CUGAUGA	Х	GAA	AUUUGCAC	GUGCAAAUU	AUGGUCUG
	543 3	ACAGACCA	CUGAUGA	X	GAA	AAUUUGCA	UGCAAAUUA	UGGUCUGU
25	5438	AGCACACA	CUGAUGA	Х	GAA	ACCAUAAU	AUUAUGGUC	UGUGUGCU
	5447	CACGACCU	CUGAUGA	X	GAA	AGCACACA	UGUGUGCUU	AGGUCGUG
	544 8	GCACGACC	CUGAUGA	Х	GAA	AAGCACAC	GUGUGCUUA	GGUCGUGC
	5452	GUGUGCAC	CUGAUGA	X	GAA	ACCUAAGC	GCUUAGGUC	GUGCACAC
	5475	CCAGCUGU	CUGAUGA	X	GAA	ACCGGCUC	GAGCCGGUC	ACAGCUGG
30	54 97	AAAGCAGC	CUGAUGA	X	GAA	AUUCAUCG	CGAUGAAUA	GCUGCUUU
	5504	CUCUCCCA	CUGAUGA	X	GAA	AGCAGCUA	UAGCUGCUU	UGGGAGAG
	55 05	GCUCUCCC	CUGAUGA	X	GAA	AAGCAGCU	AGCUGCUUU	GGGAGAGC
	5524	UAAGUGGC	CUGAUGA	Х	GAA	AGCAUGCU	AGCAUGCUA	GCCACUUA

	5531	AGAGAAUU CUGAUGA X GAA AGUGGCUA	UAGCCACUU AAUUCUCU
	5532	CAGAGAAU CUGAUGA X GAA AAGUGGCU	AGCCACUUA AUUCUCUG
	5535	GGUCAGAG CUGAUGA X GAA AUUAAGUG	CACUUAAUU CUCUGACC
	5536	CGGUCAGA CUGAUGA X GAA AAUUAAGU	ACUUAAUUC UCUGACCG
5	5538	CCCGGUCA CUGAUGA X GAA AGAAUUAA	UUAAUUCUC UGACCGGG
	5554	GUACCCAU CUGAUGA X GAA AUGCUGGC	GCCAGCAUC AUGGGUAC
	5 5 61	GGAGCAGG CUGAUGA X GAA ACCCAUGA	UCAUGGGUA CCUGCUCC
	5 56 8	ACACAGGG CUGAUGA X GAA AGCAGGUA	UACCUGCUC CCCUGUGU
	5577	GGAUGGGG CUGAUGA X GAA ACACAGGG	CCCUGUGUA CCCCAUCC
10	5584	ACCUUAAG CUGAUGA X GAA AUGGGGUA	UACCCCAUC CUUAAGGU
	5587	AAAACCUU CUGAUGA X GAA AGGAUGGG	CCCAUCCUU AAGGUUUU
	558 8	GAAAACCU CUGAUGA X GAA AAGGAUGG	CCAUCCUUA AGGUUUUC
	559 3	AGACAGAA CUGAUGA X GAA ACCUUAAG	CUUAAGGUU UUCUGUCU
	5594	CAGACAGA CUGAUGA X GAA AACCUUAA	UUAAGGUUU UCUGUCUG
15	5595	UCAGACAG CUGAUGA X GAA AAACCUUA	UAAGGUUUU CUGUCUGA '
	5596	AUCAGACA CUGAUGA X GAA AAAACCUU	AAGGUUUUC UGUCUGAU
	5600	UCUCAUCA CUGAUGA X GAA ACAGAAAA	UUUUCUGUC UGAUGAGA
	5627	UCAGUGGG CUGAUGA X GAA AUUGCACU	AGUGCAAUC CCCACUGA
	56 60	UGCACCAA CUGAUGA X GAA AGCCACAG	CUGUGGCUC UUGGUGCA
20	5662	AGUGCACC CUGAUGA X GAA AGAGCCAC	GUGGCUCUU GGUGCACU
	5671	UGGCUGGU CUGAUGA X GAA AGUGCACC	GGUGCACUC ACCAGCCA
	5685	UACUUGUC CUGAUGA X GAA AGUCCUGG	CCAGGACUA GACAAGUA
	5693	CCCUUUCC CUGAUGA X GAA ACUUGUCU	AGACAAGUA GGAAAGGG
	5704	GUGGCUAG CUGAUGA X GAA AGCCCUUU	AAAGGGCUU CUAGCCAC
25	5705	UGUGGCUA CUGAUGA X GAA AAGCCCUU	AAGGGCUUC UAGCCACA
	5707	AGUGUGGC CUGAUGA X GAA AGAAGCCC	GGGCUUCUA GCCACACU
	5731	CCCUACCU CUGAUGA X GAA AUUUUCUU	AAGAAAAUC AGGUAGGG
	5736	GCCAGCCC CUGAUGA X GAA ACCUGAUU	AAUCAGGUA GGGCUGGC
	5754	UGGACAAA CUGAUGA X GAA AUGUCUUU	AAAGACAUC UUUGUCCA
30 .	5756	AAUGGACA CUGAUGA X GAA AGAUGUCU	AGACAUCUU UGUCCAUU
	5757	GAAUGGAC CUGAUGA X GAA AAGAUGUC	GACAUCUUU GUCCAUUC
	5760	UGCGAAUG CUGAUGA X GAA ACAAAGAU	AUCUUUGUC CAUUCGCA
	5764	CUUUUGCG CUGAUGA X GAA AUGGACAA	UUGUCCAUU CGCAAAAG

	5765	GCUUUUGC	CUGAUGA	X	GAA	AAUGGACA	UGUCCAUUC	GCAAAAGC
	577 5	GCCGACAA	CUGAUGA	X	GAA	AGCUUUUG	CAAAAGCUC	UUGUCGGC
	5777	CAGCCGAC	CUGAUGA	x	GAA	AGAGCUUU	AAAGCUCUU	GUCGGCUG
	5 78 0	CUGCAGCC	CUGAUGA	Х	GAA	ACAAGAGC	GCUCUUGUC	GGCUGCAG
5	5794	GCCUGACU	CUGAUGA	X	GAA	ACACACUG	CAGUGUGUA	AGUCAGGC
	5798	CAUCGCCU	CUGAUGA	X	GAA	ACUUACAC	GUGUAAGUC	AGGCGAUG
	5818	UUCUCUGG	CUGAUGA	x	GAA	AGCCUCUG	CAGAGGCUA	CCAGAGAA
	5852	GGAUGAGA	CUGAUGA	X	GAA	ACCUCAGG	CCUGAGGUU	UCUCAUCC
	585 3	UGGAUGAG	CUGAUGA	x	GAA	AACCUCAG	CUGAGGUUU	CUCAUCCA
10	5854	CUGGAUGA	CUGAUGA	·x	GAA	AAACCUCA	UGAGGUUUC	UCAUCCAG
	5856	AUCUGGAU	CUGAUGA	х	GAA	AGAAACCU	AGGUUUCUC	AUCCAGAU
	5859	GAUAUCUG	CUGAUGA	Х	GAA	AUGAGAAA	UUUCUCAUC	CAGAUAUC
	5865	UUGCUGGA	CUGAUGA	x	GAA	AUCUGGAU	AUCCAGAUA	UCCAGCAA
	5867	AAUUGCUG	CUGAUGA	X	GAA	AUAUCUGG	CCAGAUAUC	CAGCAAUU
15	587 5	CACCCCCC	CUGAUGA	х	GAA	AUUGCUGG	CCAGCAAUU	GGGGGGUG
	5896	GGACCAUC	CUGAUGA	X	GAA	AUGGUCUU	AAGACCAUA	GAUGGUCC
	5903	UAAUACAG	CUGAUGA	x	GAA	ACCAUCUA	UAGAUGGUC	CUGUAUUA
	5908	CGGAAUAA	CUGAUGA	X	GAA	ACAGGACC	GGUCCUGUA	UUAUUCCG
	5910	AUCGGAAU	CUGAUGA	х	GÀA	AUACAGGA	UCCUGUAUU	AUUCCGAU
20	5911	AAUCGGAA	CUGAUGA	X	GAA	AAUACAGG	CCUGUAUUA	UUCCGAUU
	5913	AAAAUCGG	CUGAUGA	х	GAA	AUAAUACA	UGUAUUAUU	CCGAUUUU
	5914	UAAAAUCG	CUGAUGA	X	GAA	AAUAAUAC	GUAUUAUUC	CGAUUUUA
	5919	AAUUAUUA	CUGAUGA	х	GAA	AUCGGAAU	AUUCCGAUU	UUAAUAAU
	5920	GAUUAUUA	CUGAUGA	X	GAA	AAUCGGAA	UUCCGAUUU	UAAUAAUC
25	5921	AGAUUAUU	CUGAUGA	X	GAA	AAAUCGGA	UCCGAUUUU	AAUAAUCU
	5922	UAGAUUAU	CUGAUGA	X	GAA	AAAAUCGG	CCGAUUUUA	AUAAUCUA
	592 5	AAUUAGAU	CUGAUGA	Х	GAA	UAAAAU	AUUUUUAAUA	AUCUAAUU
	5928	ACGAAUUA	CUGAUGA	Х	GAA	AAUUAUUA	UUAAUAAUC	UAAUUCGU
	5930	UCACGAAU	CUGAUGA	X	GAA	AGAUUAUU	AAUAAUCUA	AUUCGUGA
30	5933	UGAUCACG	CUGAUGA	X	GAA	AUUAGAUU	AAUCUAAUU	CGUGAUCA
	5934	AUGAUCAC	CUGAUGA	Х	GAA	AAUUAGAU	AUCUAAUUC	GUGAUCAU
	5940	CUCUUAAU	CUGAUGA	X	GAA	AUCACGAA	UUCGUGAUC	AUUAAGAG
	594 3	AGUCUCUU	CUGAUGA	Х	GAA	AUGAUCAC	GUGAUCAUU	AAGAGACU

	5944	AAGUCUCU	CUGAUGA	X	GAA	AAUGAUCA	UGAUCAUUA AGAGACUU
	5952	AUUUACUA	CUGAUGA	X	GAA	AGUCUCUU	AAGAGACUU UAGUAAAU
	5953	CAUUUACU	CUGAUGA	X	GAA	AAGUCUCU	AGAGACUUU AGUAAAUG
	5954	ACAUUUAC	CUGAUGA	Х	GAA	AAAGUCUC	GAGACUUUA GUAAAUGU
5	59 57	GGGACAUU	CUGAUGA	Х	GAA	ACUAAAGU	ACUUUAGUA AAUGUCCC
	59 63	GGAAAAGG	CUGAUGA	Х	GAA	ACAUUUAC	GUAAAUGUC CCUUUUCC
	5967	UGUGGGAA	CUGAUGA	X	GAA	AGGGACAU	AUGUCCCUU UUCCCACA
	5968	UUGUGGGA	CUGAUGA	X	GAA	AAGGGACA	UGUCCCUUU UCCCACAA
	5969	UUUGUGGG	CUGAUGA	X	GAA	AAAGGGAC	GUCCCUUUU CCCACAAA
10	5970	UUUUGUGG	CUGAUGA	X	GAA	AAAAGGGA	UCCCUUUUC CCACAAA
	5981	CUUUUCUU	CUGAUGA	X	GAA	ACUUUUGU	ACAAAAGUA AAGAAAAG
	5 9 92	AAUCCCGA	CUGAUGA	X	GAA	AGCUUUUC	GAAAAGCUA UCGGGAUU
	5994	AGAAUCCC	CUGAUGA	Х	GAA	AUAGCUUU	AAAGCUAUC GGGAUUCU
	600 0	AACCAGAG	CUGAUGA	X	GAA	AUCCCGAU	AUCGGGAUU CUCUGGUU
15	6001	GAACCAGA	CUGAUGA	X	GAA	AAUCCCGA	UCGGGAUUC UCUGGUUC
	60 03	CAGAACCA	CUGAUGA	X	GAA	AGAAUCCC	GGGAUUCUC UGGUUCUG.
	6008	UUAAGCAG	CUGAUGA	X	GAA	ACCAGAGA	UCUCUGGUU CUGCUUAA
	600 9	UUUAAGCA	CUGAUGA	X	GAA	AACCAGAG	CUCUGGUUC UGCUUAAA
	6014	AAGUCUUU	CUGAUGA	X	GAA	AGCAGAAC	GUUCUGCUU AAAGACUU
20	6015	UAAGUCUU	CUGAUGA	X	GAA	AAGCAGAA	UUCUGCUUA AAGACUUA
	6022	CCAAAGCU	CUGAUGA	X	GAA	AGUCUUUA	UAAAGACUU AGCUUUGG
	6023	UCCAAAGC					AAAGACUUA GCUUUGGA
	6027	AGGCUCCA					ACUUAGCUU UGGAGCCU
	6028	UAGGCUCC					CUUAGCUUU GGAGCCUA
25	6036	AACUUUCA					UGGAGCCUA UGAAAGUU
	6044	GGCUGAUC	CUGAUGA :	X	GAA	ACUUUCAU	AUGAAAGUU GAUCAGCC

Where "X" represents stem II region of a HH ribozyme (Hertel et al., 1992 Nucleic Acids Res. 20 3252). The length of stem II may be \geq 2 base-pairs.

184

Table IX: Mouse flt1 VEGF Receptor-Hairpin Ribozyme and Substrate Sequence

Ŋ

Seduence	Substrate			A AUGGUCA GCU GCUGGGAC	A GUCAGCU GCU GGGACACC	A CACCGCG GUC UUGCCUUA	ACGCGCU GCU CGGGUGUC	GGUGUCU GCU UCUCACAG	CAGGCCA GAC UCUCUTUC	GGAGGCA GCC CACUCAUG	GGUCUCU GCC CACGACCG	cccauce ecc ususesas	GAAGACA GCU CAUCAUCC	AUCCCCU GCC GGGUGACG	. UACCCCU GAU GGGCAAAG	UAGGACU GCU GAACUGCG	ACUAUCU GAC CCAUCGGC	AUCGGCA GAC CAAUACAA
lable 1X: Mouse IIII VEGF Receptor-Hairpin Ribozyme and Substrate Sequence	HP Ribozyme Sequence			GUCCCAGC AGAA GACCAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GGUGUCCC AGAA GCUGAC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UAAGGCAA AGAA GCGGUG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	GACACCCG AGAA GCGCGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CUGUGAGA AGAA GACACC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GAAAGAGA AGAA GGCCUG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CAUGAGUG AGAA GCCUCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CGGUCGUG AGAA GAGACC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CUCCCACA AGAA GAUGGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GGAUGAUG AGAA GUCUUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CGUCACCC AGAA GGGGAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CUUUGCCC AGAA GGGGUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CGCAGUUC AGAA GUCCUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GCCGAUGG AGAA GAUAGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UUGUAUUG AGAA GCCGAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA
Table	nt.	Posi-	tion	33	36	20	67	79	166	197	214	266	487	501	266	640	691	703

185

UACGCCC GCC GAGCCCAG ACGGGCA GAC UCUUGUCC GCGUGAAG CGUUCCA GUC UUUCAACA UGAGACU GCU CCACGGGC GAU UGACCGGA GGUGCAGG AUCGGCU GUC CAUGAAAG CCUAUCG GCU GUCCAUGA GAAGUCU GCU CGCUAUUU UCUAUCC GCU GGGCAGCA CUAUCGGC CUACGAAA UCUCAGAC CCCUGGAA BCCGGGCC GGGCCNNC GUGCCGAA GAAGGAGA CC UACACCU GUC GNC GAU GAC GAU ggg GAC AUCUACA GCU UACAGCU GCC GGCAGCG GGAAGCA GAAGACG AACCUCA GGUGGCU ACUCUCA GAUGCCA UGUCACA CUGGGCUC AGAA GGCGUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA GCCCGU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GCUGCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CUUCACGC AGAA GGUGUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGAACG ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA GCUUCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GAUAGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCCGAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUCUUC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA AAAUAGCG AGAA GACUUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UUUCGUAG AGAA GAGGUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAUAGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUCUGAGA AGAA GCCACC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AGAA GAGAGU ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA GUAGAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAAGGCCC AGAA GCUGUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AGAA GUGACA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA GGCAUC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GUCUCA AGAA JGUUGAAA AGAA GGACAAGA AGAA UCCGGUCA AGAA GCCGAUAG AGAA AGAA CCUGCACC AGAA CUUUCAUG AGAA UGCUGCCC AGAA UCUCCUUC AGAA GGCCCGGC AGAA SCCCGNGG UCAUGGAC UUCCAGGG JUCGGCAC 1169 1051 1090 1093 1315 1363 1612 1629 1081 1604 1688 1632 1730 736 991 988 754 871 960

1.0

15

BNSDOCID: <WO___9715662A2_I_>

S

JA CACACCU GCU UCAAAACC	JA CGCCUCA GAU CACUUGGU	JA GCACGCU GUU UAUUGAAA	JA AAGCGCA GCC UACCUCAC	JA UGGAGCU GAU CACGCUCA	M UGAAGCG GUC UUCUUCCG	A AAAGACA GAC UACCUGUC	A GGACCCA GAU GAAGUUCC	GUGAACG GCU GCCCUAUG	A AACGGCU GCC CUAUGAUG	A CCCACCU GCC GGACUGUG	A CCUGCCG GAC UGUGGCUG	A AAGCUCU GAU GACCGAAC	A GGCCUCU GAU GGUGAUCG	A GAAACCU GUC CAACUACC	A UVAUUCU GUC UCAACAAG	A GGACGCA GCC UUGCAUAU	A AAGCCCC GCC UAGACAGU
GGUGUG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	3AGGCG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GCGUGC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	GCGCUU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	SCUCCA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	SCUUCA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	GUCUUU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	3GGUCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	JUUCAC ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	3CCGUU ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	BGUGGG ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	GCAGG ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	AGCUU ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	AGGCC ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	GUUUC ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	BANDAA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	ICGUCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	GGCUU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA
	AGAA (AGAA (AGAA (AGAA (AGAA (AGAA (AGAA (AGAA (AGAA (AGAA C	AGAA C	AGAA C	AGAA C	AGAA G	AGAA G	AGAA G	AGAA G
GGUUUUGA AGAA	ACCAAGUG AGAA GAGGCG	UUUCAAUA AGAA	GUGAGGUA AGAA	UGAGCGUG AGAA GCUCCA	CGGAAGAA AGAA GCUUCA	GACAGGUA AGAA	GGAACUUC AGAA GGGUCC	CAUAGGGC AGAA GUUCAC	CAUCAUAG AGAA GCCGUU	CACAGUCC AGAA GGUGGG	CAGCCACA AGAA GGCAGG	GUUCGGUC AGAA GAGCUU	CGAUCACC AGAA GAGGCC	GGUAGUUG AGAA GGUUUC	CUUGUUGA AGAA GAAUAA	AUAUGCAA AGAA GCGUCC	ACUGUCUA AGAA GGGCUU
2017	2101	2176	2258	2305	2383	2405	2432	2464	2467	2592	2596	2653	2743	2779	2814	2831	2895
			5					10					15				

								1	87									
GUCAGCA GCU CAAGUGUC	GUCACCA GCU CCAGCUUC	AGCUCCA GCU UCCCUGAA	CCAAGCA GCC CCUCACCA	AAGACCU GAU UUCCUACA	UCCUACA GUU UCCAAGUG	AGUUUCU GUC CUCCAGAA	GAACCCU GAU UAUGUGAG	UUCUGCA GCC GCCUGAAG	UGCAGCC GCC UGAAGGAA	GCAUGCG GAU GAGAACCC	GGCCCCG GUN UGCUGAAC		CCAUACU GAC UAGAAACA	AAGGACG GCU UUGCAGAU	CUTUGCA GAU CCACATHITI		ACUAUCA GCU GGACACIJA	GCACUCU GCU GGGCUCCC
GACACUUG AGAA GCUGAC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GAAGCUGG AGAA GGUGAC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UUCAGGGA AGAA GGAGCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UGGUGAGG AGAA GCUUGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UGUAGGAA AGAA GGUCUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CACUUGGA AGAA GUAGGA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UUCUGGAG AGAA GAAACU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CUCACAUA AGAA GGGUUC ACCAGAGAAACACGCUUGUGGUACAUUACCUGGUA	CUUCAGGC AGAA GCAGAA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UUCCUUCA AGAA GCUGCA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	GGGUUCUC AGAA GCAUGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GUUCAGCA AGAA GGGGCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	UGGCUUGA AGAA GGUCAC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UGUUUCUA AGAA GUAUGG ACCAGAGAAACACGCUUGUGGUACAUUACCUGGUA	AUCUGCAA AGAA GUCCUU ACCAGAGAAACACGCUUGUGGUACAUUACCUGGUA	AAAUGUGG AGAA GCAAAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CUCACAUC AGAA GAGCUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UAGUGUCC AGAA GAUAGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GGGAGCCC AGAA GAGUGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA
2913	2928	2934	3001	5 3022	3033	3064	3179	3357	10 3360	3379	3463	3496	3553	15 3615	3623	3650	3754	3772

	ACCGCCC GCC CACCGGCC	GGCCGGUG AGAA GGCGGU	4294
	GGCGACC GCC CGCCCACC	GGUGGGCG AGAA GUCGCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	4290
	UGUUGCU GUU UUGACUAA	UVAGUCAA AGAA GCAACA ACCAGAGAAACACGUUGUGGUACAUVACCUGGUA	4168
	GCCAGCU GCU UUUCGUGA	UCACGAAA AGAA GCUGGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	4113
	GGAGCCA GCU GCUUUUCG	CGAAAAGC AGAA GGCUCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	4110
	CUAUUCC GCU CCACAGGA	UCCUGUGG AGAA GAAUAG ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	4095
	ACAACCA GCC CCUGACAG	CUGUCAGG AGAA GGUUGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	4053
	CUCACCA GCC CCGACAAC	GUUGUCGG AGAA GGUGAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	4040
	CCCGCCC GCC UAAAGCUU	AAGCUUUA AGAA GGCGGG ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	4022
188	CCUCCCC GCC CGCCUAAA	UUUAGGCG AGAA GGGAGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	4018
	ACCCCCA GAC UACAACUC	GAGUUGUA AGAA GGGGGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	3986
-	uccugcu guu cuccaccc	GGGUGGAG AGAA GCAGGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	3972
	GAGUCCU GCU GUUCUCCA	UGGAGAAC AGAA GGACUC ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	3969
	UUCUCCA GCU GUGGCCAC	GUGGCCAC AGAA GGAGAA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	3912
	AGCUUCU GCU UCUCCAGC	GCUGGAGA AGAA GAAGCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	3903
	AGGCCCA GCU UCUGCUUC	GAAGCAGA AGAA GGGCCU ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	3897
	CCGAUCU GCC GAGGCCCA	UGGGCCUC AGAA GAUCGG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	3886
	ACUUUCC GAU CUGCCGAG	CUCGGCAG AGAA GAAAGU ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	3881
	UGAAGCG GUU CACCUGGA	UCCAGGUG AGAA GCUUCA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	3796

GEUGCEC GEU CUUUGGGG

CCCCAAAG AGAA GGCACC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

5363

	4329	AGUCCCAC AGE	AA GCAGGG	AGUCCCAC AGAA GCAGGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CCCUGCA GCU GUGGGACU
	4378	CAGAGCAG AGAA GUGCAU	AA GUGCAU	ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	AUGCACU GAC CUGCUCUG
	4383	AGAGACAG AGAA GGUCAG	AA GGUCAG	ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CUGACCU GCU CUGUCUCU
	4388	AUAAGAGA AGAA GAGCAG	AA GAGCAG	ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CUGCUCU GUC UCUCUUAU
2	4457	CUCCACAG AGAA GACGCA	A GACGCA		UGCGUCC GUC CUGUGGAG
	4525	CCCGAAAC AGAA GAGGCC	AA GAGGCC	ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	eeccncc ecn ennaceee
	4528	GGGCCCGA AGAA GCGGAG	AA GCGGAG	ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	cnccecn enn nceeeccc
	4643	AAACAGAC AGAA GAAGAC	A GAAGAC	ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	GUCUNCO GUU GUCUGUUN
	4650	GGAUGGUA AGAA GACAAC	A GACAAC	ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	GUUGUCU GUU NACCAUCC
0	4724	ACUAGAGG AGAA GAUGAU	A GAUGAU	ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	AUCAUCA GUU CCUCUAGU
	4771	AUGCGAAG AGAA GGCCUG	A GGCCUG	ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	
	4785	UCCCCGUG AGAA GUAUGC	A GUAUGC	ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	GCAUACU GCU CACGGGGA
	4809	CUAGGCCA AGAA GGACCA	A GGACCA	ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UGGUCCA GUU UGGCCUAG
	4834	UUGAGCCC AGAA GUAGGC	A GUAGGC	ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	GCCUACU GAU GGGCUCAA
S	4912	AUAUAUAA AGAA GGAUAA		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UUAUCCU GUU UUAUAUAU
	5119	UCCUCUCA AGAA GCCUUG		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CAAGGCA GUC UGAGAGGA
	5144	UAAAUAUG AGAA GAUACU		ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	AGUAUCA GCC CAUAUUUA
	5287	AGGUAUGA AGAA GAUGAA		ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	UUCAUCU GUU UCAUACCII
	1				

	5462	CCGGCUCC AGAA GGUGUG ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CACACCU GCC GGAGCCGG
	5478	GUCUGCCC AGAA GUGACC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GGUCACA GCU GGGCAGAC
	5486	UAUUCAUC AGAA GCCCAG ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	CUGGGCA GAC GAUGAAUA
	5500	UCUCCCAA AGAA GCUAUU ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	AAUAGCU GCU UUGGGAGA
5	5539	CUGGCCCG AGAA GAGAAU ACCAGAGAAACACAUGUGUGGUACAUUACCUGGUA	AUUCUCU GAC CGGGCCAG
	5564	CACAGGGG AGAA GGUACC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GGUACCU GCU CCCCUGUG
	5597	UCUCAUCA AGAA GAAAAC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GUTUUCU GUC UGAUGAGA
	5601	CCAGUCUC AGAA GACAGA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UCUGUCU GAU GAGACUGG
	5639	GGGCUGCA AGAA GUCUCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UGAGACA GCC UGCAGCCC
10	5646	CCACAGUG AGAA GCAGGC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	GCCUGCA GCC CACUGUGG
	5781	CACACUGC AGAA GACAAG ACCAGAGAACACGCUGUGGUACAUUACCUGGUA	CUUGUCG GCU GCAGUGUG
	5829	CUGUUCUC AGAA GUUUCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	AGAAACG GAU GAGAACAG
	5842	AAACCUCA AGAA GCUGUU ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	AACAGCA GCC UGAGGUUU
	5915	UUAUUAAA AGAA GAAUAA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	UVAUUCC GAU UUUAAUAA
1.5	6010	AGUCUTUDA AGAA GAACCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UGGUUCU GCU UAAAGACU

WO 97/15662 PCT/US96/17480

Table X: Homologous Hammerhead Ribozyme Target Sites
Between Human flt-1 and KDR RNA

	nt.	flt-1	nt.	KDR
	Posi-	Target Sequence	Posi-	Target Sequence
5	tion		tion	
	3388	CCGGGAU A UUUAUAA	3151	CCGGGAU A UUUAUAA
	2174	AAUGUAU A CACAGGG	3069	Aguguau c Cacaggg
	2990	UGCAAAU A UGGAAAU	2756	UGCAAAU u UGGAAAc
	2693	CUCCCUU A UGAUGCC	2459	CUGCCUU A UGAUGCC
10	2981	GUUGAAU A CUGCAAA	2747	GUgGAAU u CUGCAAA
	1359	UAUGGUU A AAAGAUG	2097	UgUGGUU u AAAGAUa
	3390	GGGAUAU U UAUAAGA	3153	GGGAUAU U UAUAAag
	3391	GGAUAUU U AUAAGAA	3154	GGAUAUU U AUAAagA
	2925	ACGUGGU U AACCUGC	2691	AuGUGGU c AACCUuC
15	7140	UAUUUCU A GUCAUGA	2340	UACUUCU u GUCAUCA
	1785	CAAUAAU A GAAGGAA	1515	CucUAAU u GAAGGAA
	2731	GAGACUU A AACUGGG	768	uuGACUU c AACUGGG
	3974	GAUGACU A CCAGGGC	1466	GAgGACU u CCAGGGa
	6590	UUAAUGU A GAAAGAA	2603	aaAAUGU u GAAAGAA
20	6705	GCCAUUU A UGACAAA	3227	aCaAUUU u UGACAgA
	974	GUCAAAU U ACUUAGA	147	uUCAAAU U ACUUgcA
	1872	AUAAAGU U GGGACUG	1602	AcAAAGU c GGGAgaG
	2333	ACUUGGU U UAAAAAC	1088	AaaUGGU a UAAAAAu
	2775	AAGUGGU U CAAGCAU	1745	AcaUGGU a CAAGCuU
25	3533	UUCUCCU U AGGUGGG	3296	UUuUCCU U AGGUGcu
	3534	UCUCCUU A GGUGGGU	3297	UuUCCUU A GGUGcuU
	3625	GUACUCU A CUCCUGA	4054	GagCUCU c CUCCUGu
	1814	AGCACCU U GGUUGUG	1059	AGuACCU U GGUUacc
	2744	GGCAAAU C ACUUGGA	147	uuCAAAU u ACUUGcA
30	2783	CAAGCAU C AGCAUUU	796	gAAGCAU C AGCAUaa

	3613	GAGAGCU (CUGAGUA	2968	GgaAGCU C CUGAagA
	4052	AAGGCCU (GCUCAAG	1923	ucuGCCU u GCUCAAG
	5305	UCUCCAU A	A UCAAAAC	456	ggUCCAU u UCAAAuC
	7158	AUGUAUU U	J UGUAUAC	631	gUcUAUU a UGUAcAu
5	1836	CUAGAAU t	J UCUGGAA	1007	aUgGAAU c UCUGGug
	2565	CUCUCUU (UGGCUCC	2328	uguUCUU C UGGCUaC
	4250	CUGUACU (CACCCCA	3388	uUaUACU a CACCagA
	7124	ACAUGGU U	J UGGUCCU	3778	cagUGGU a UGGUuCU
	436	AUGGUCU U	UGCCUGA	1337	AcGGUCU a UGCCauu
10	2234	GCACCAU A	CCUCCUG	1344	augCCAU u CCUCCcc
	2763	GGGCUUU U	J GGAAAAG	990	uuGCUUU U GGAAguG
	4229	CCAGACU A	CAACUCG	767	auuGACU u CAACUgG
	5301	GUUUUCU C	CAUAUCA	3307	ugcUUCU C CAUAUCc
	6015	AGAAUGU A	UGCCUCU	1917	AcuAUGU c UGCCUug
15	6095	AUUCCCU A	GUGAGCC	1438	AUaCCCU u GUGAaga
	6236	UGUUGUU C	CUCUUCU	76	UagUGUU u CUCUUga
	5962	GCUUCCU U	UUAUCCA	3099	auaUCCU c UUAUCgg
	7629	UAUAUAU U	CUCUGCU	3096	gAaAUAU c CUCUuaU

Lowercase letters are used to represent sequence variance 20 between flt-1 and KDR RNA

193

	Table XI: 2.5 μ mol	RNA Synthesis	Cycle	
	Reagent	Equivalents	Amount	Wait Time*
	Phosphoramidites	6.5	163 <i>µ</i> L	2.5
	S-Ethyl Tetrazole	23.8	238µL	2.5
5	Acetic Anhydride	100	233 μL	5 se c
	N-Methyl Imidazole	186	233 μL	5 se c
	TCA	83.2	1.73 mL	21 sec
	Iodine	8.0	1.18 mL	45 se c
	Acetonitrile	NA	6.67 ml	NA

Claims

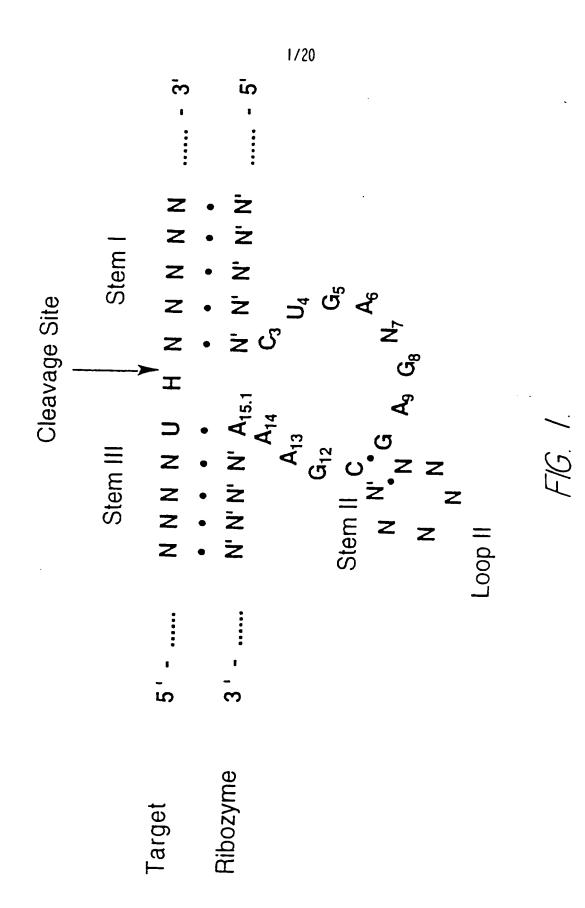
- 1. Nucleic acid molecule which modulates the synthesis, expression and/or stability of an mRNA encoding one or more receptors of vascular endothelial growth factor.
 - 2. The nucleic acid of claim 1, wherein said receptor is flt-1, KDR and/or flk-1.
 - 3. The nucleic acid of claim 1 or 2, wherein said molecule is an enzymatic nucleic acid molecule.
- 4. The nucleic acid molecule of claim 3, wherein, the binding arms of said enzymatic nucleic acid contain sequences complementary to the substrate nucleotide base sequences in any one of Tables II to IX.
- The nucleic acid molecule of claims 3 or 4,
 wherein said nucleic acid molecule is in a hammerhead motif.
- 6. The enzymatic nucleic acid molecule of claim 3 or 4, wherein said nucleic acid molecule is in a hairpin, hepatitis Delta virus, group I intron, VS nucleic acid or 20 RNaseP nucleic acid motif.
 - 7. The enzymatic nucleic acid molecule of any of claims 3 or 4, wherein said ribozyme comprises between 12 and 100 bases complementary to the RNA of said region.
- 8. The enzymatic nucleic acid of claim 7, wherein 25 said ribozyme comprises between 14 and 24 bases complementary to the RNA of said region.
 - 9. Enzymatic nucleic acid molecule consisting essentially of any ribozyme sequence selected from those shown in Tables II to IX.

WO 97/15662 PCT/US96/17480

- 10. A mammalian cell including a nucleic acid molecule of any of claims 1, 2 or 3.
- 11. The cell of claim 10, wherein said cell is a human cell.
- 12. An expression vector comprising nucleic acid encoding the nucleic acid molecule of any of claims 1, 2, 3 or 4, in a manner which allows expression and/or delivery of that RNA molecule within a mammalian cell.
- 13. The expression vector of claim 12, wherein said 10 nucleic acid is an enzymatic nucleic acid.
 - 14. A mammalian cell including an expression vector of any of claims 12 or 13.
 - 15. The cell of claim 14, wherein said cell is a human cell.
- 16. A method for treatment of a patient having a condition associated with the level of flt-1, KDR and/or flk-1, wherein the patient, tissue donor or population of corresponding cells is administered a therapeutically effective amount of an enzymatic nucleic acid molecule of claims 1, 2, 3 or 4.
 - 17. A method for treatment of a condition related to the level of flt-1, KDR and/or flk-1 activity by administering to a patient an expression vector of claim 12.
- 18. The method of claims 16 or 17, wherein said 25 patient is a human.
 - 19. The nucleic acid of claim 1 or 2, wherein said molecule is an antisense nucleic acid molecule.

WO 97/15662 PCT/US96/17480

- 20. The nucleic acid molecule of claim 19, wherein, said antisense nucleic acid contain sequences complementary to the substrate nucleotide base sequences in any one of Tables II to IX.
- 21. An expression vector comprising nucleic acid encoding the antisense nucleic acid molecule of any one of claims 19 or 20, in a manner which allows expression and/or delivery of that antisense RNA molecule within a mammalian cell.
- 10 22. A mammalian cell including an expression vector of claim 21.
 - 23. The cell of claim 22, wherein said cell is a human cell.



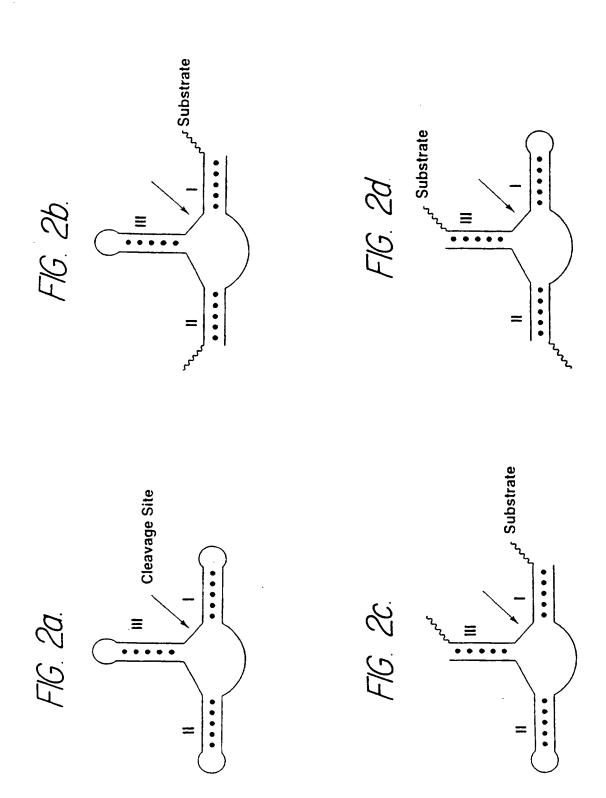
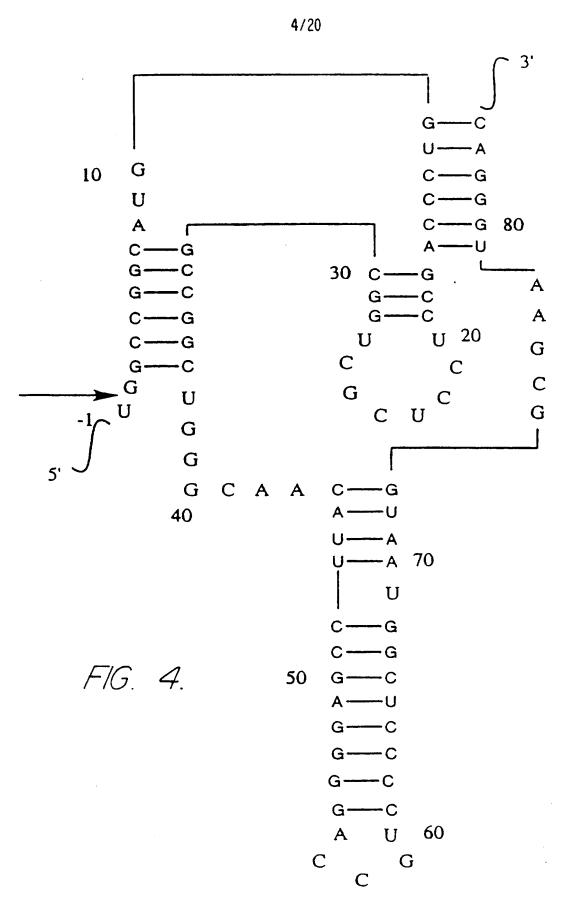


FIG. 3.



NEUROSPORA VS RNA ENZYME

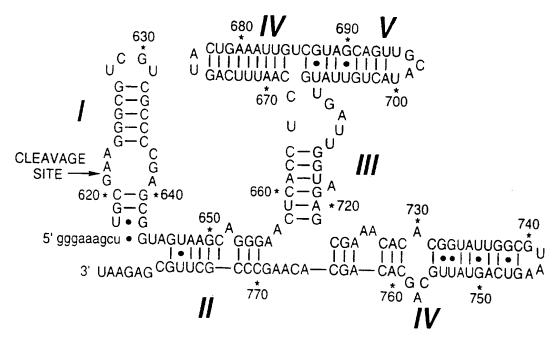
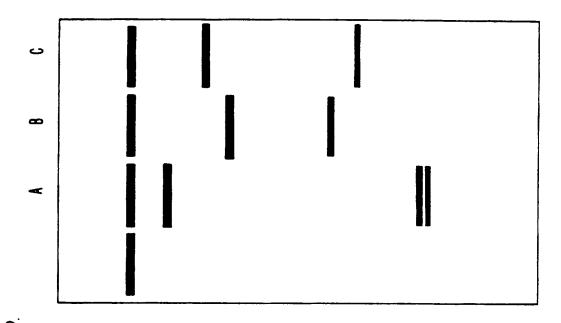
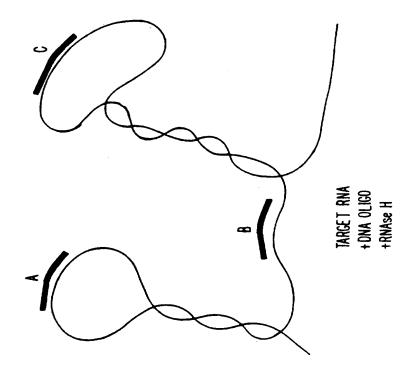


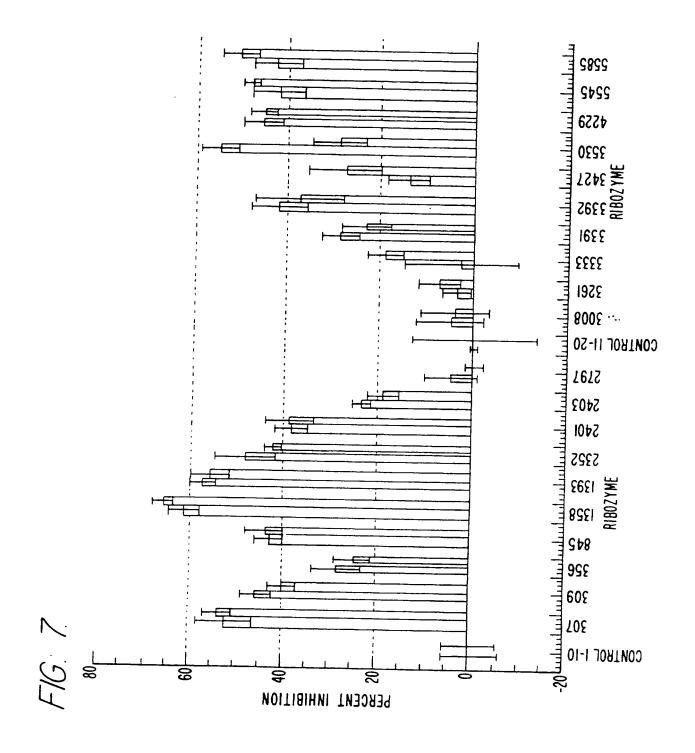
FIG. 5.

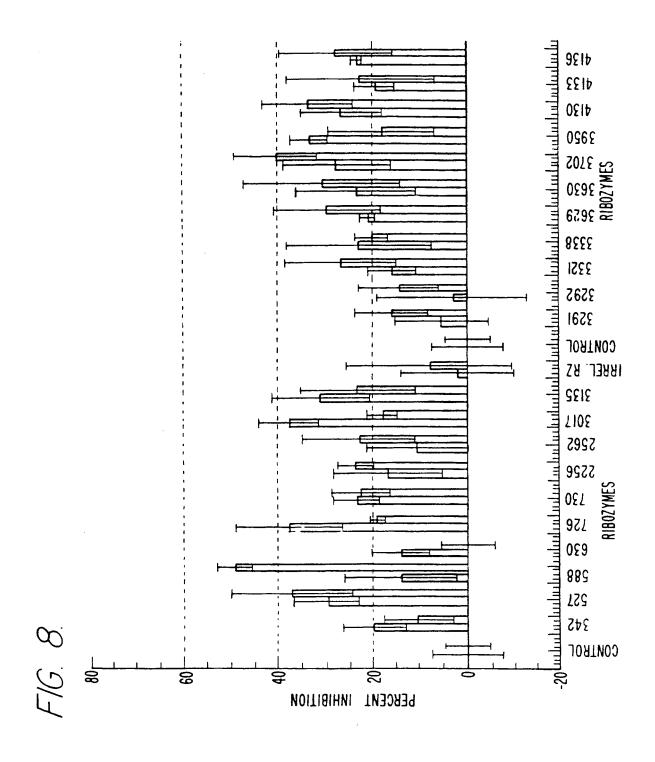


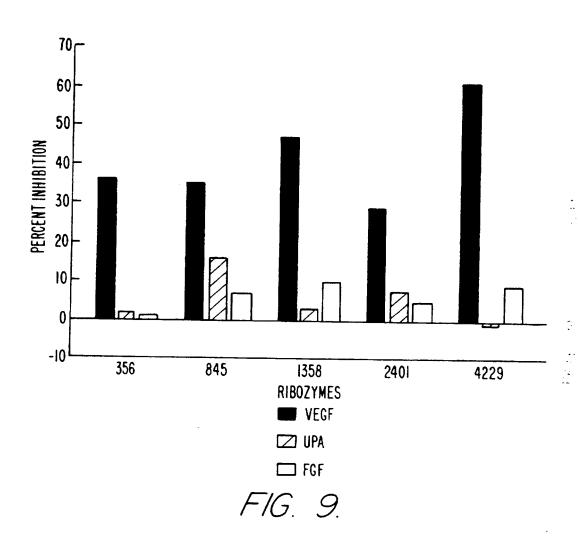
·16. 6

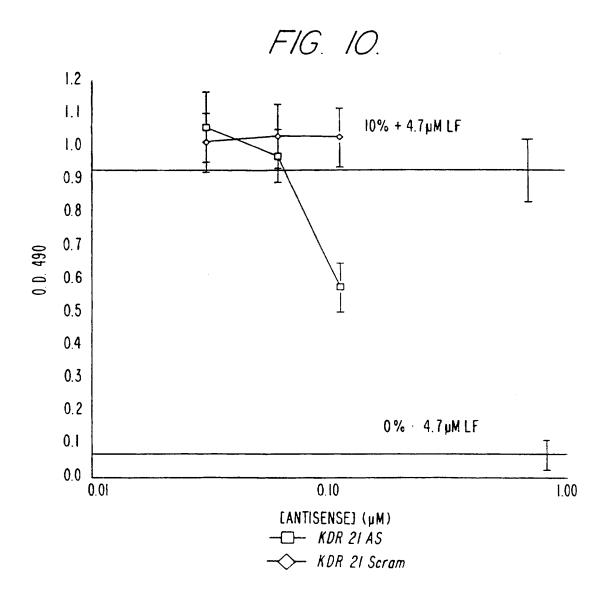


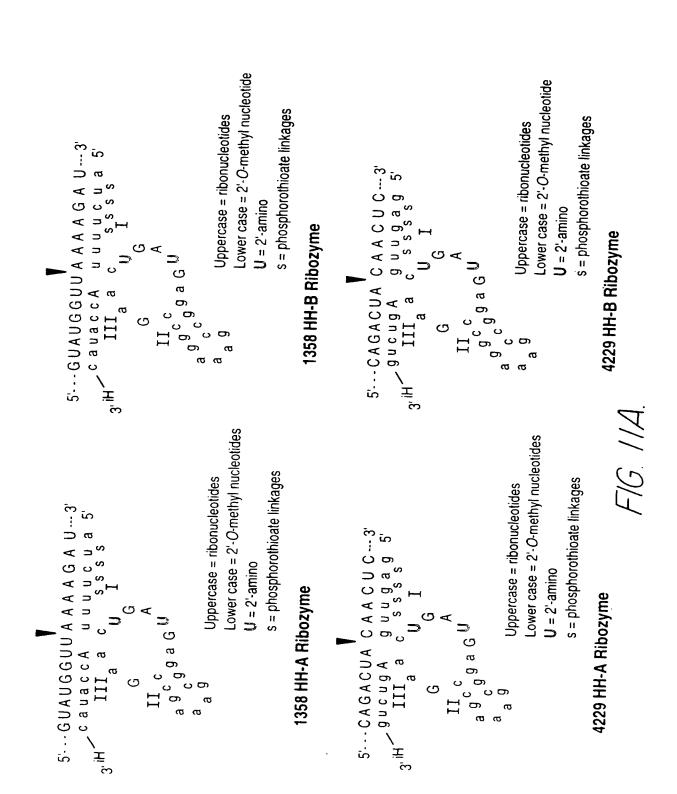
7/20











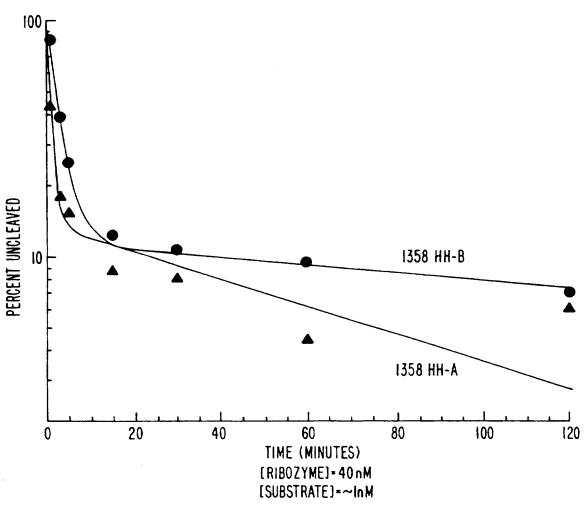
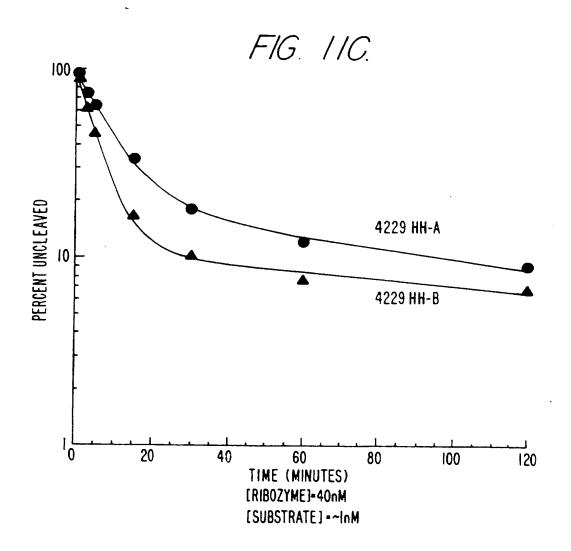
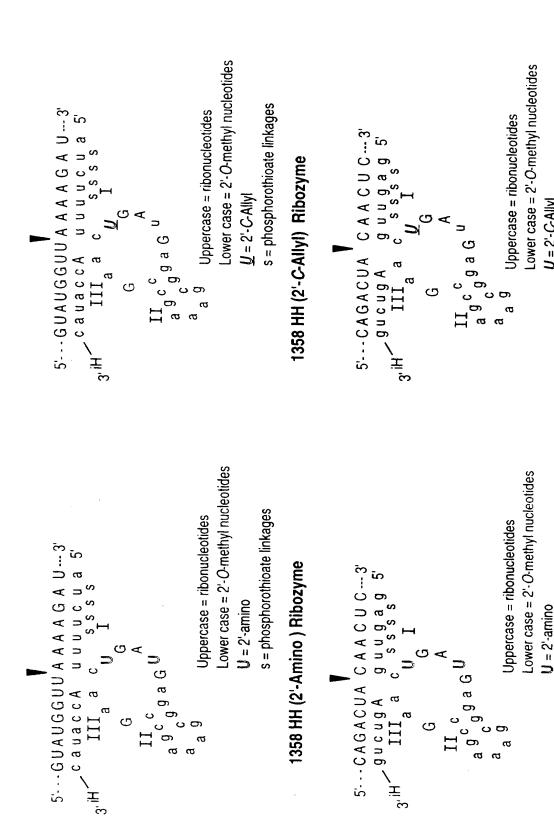


FIG. 11B.





4229 HH (2'-CAllyl) Ribozyme

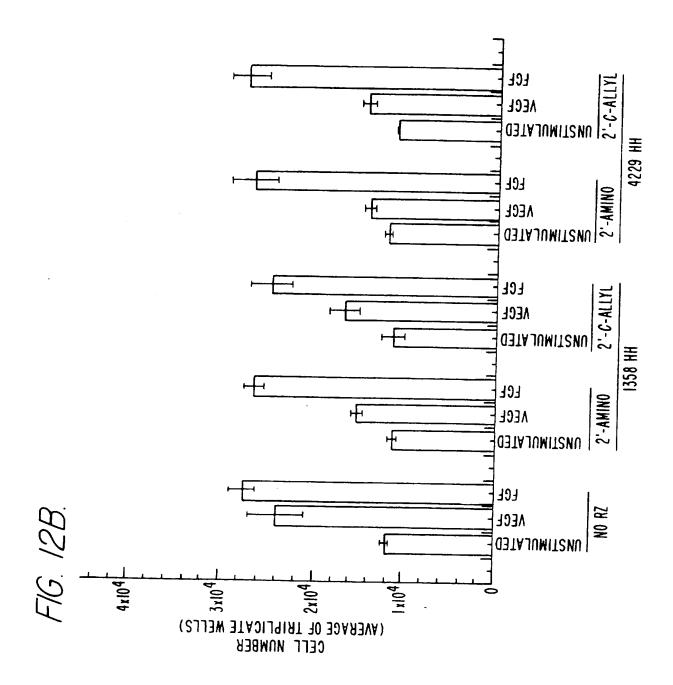
s = phosphorothioate linkages

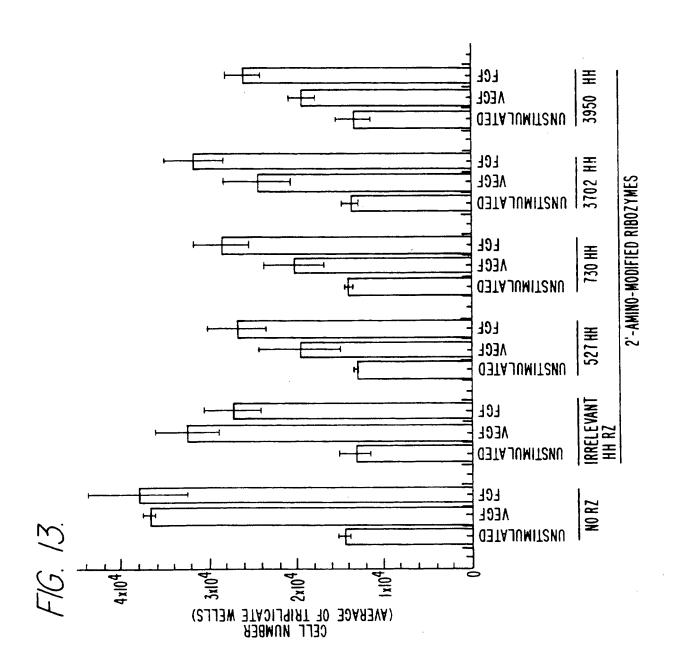
s = phosphorothioate linkages

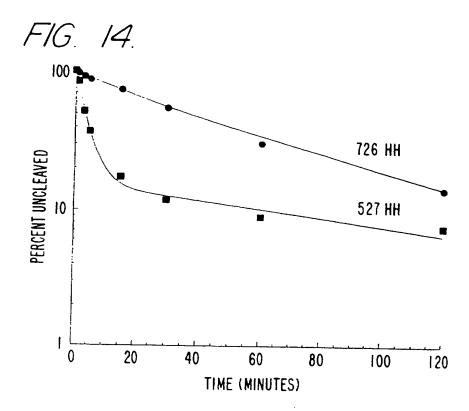
4229 HH (2'-Amino) Ribozyme

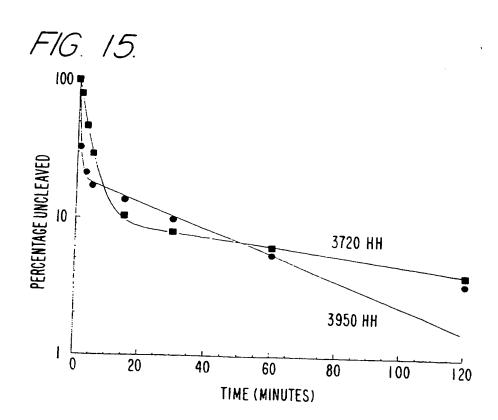
-7*G. 12*4.

SUBSTITUTE SHEET (RULE 26)

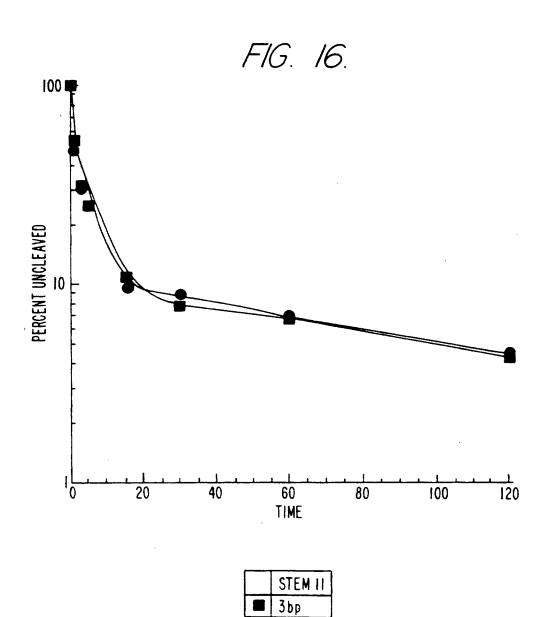






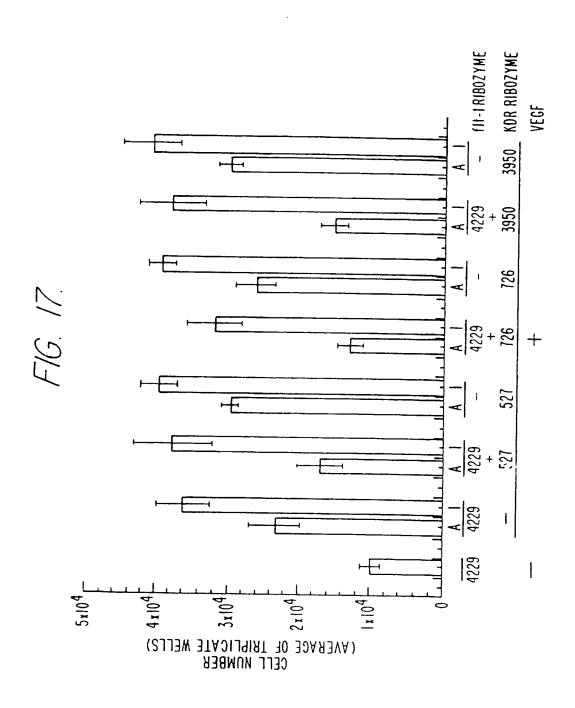


SUBSTITUTE SHEET (RULE 26)

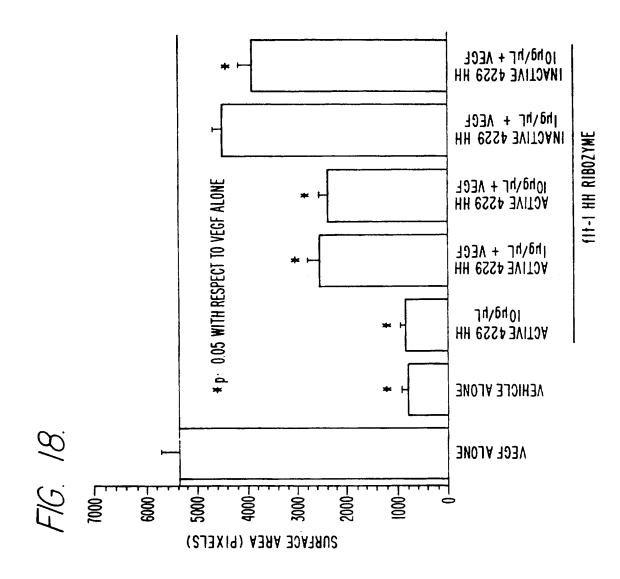


SUBSTITUTE SHEET (RULE 26)

4 bp



SUBSTITUTE SHEET (RULE 26)



SUBSTITUTE SHEET (RULE 26)

WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



(51) International Patent Classification 6:		(11) International Publication Number:	WO 97/15662
C12N 15/11, 9/00, 5/10	A3	(43) International Publication Date:	1 May 1997 (01.05.97
(21) International Application Number: PCT/US (22) International Filing Date: 25 October 1996 (2)		BE, CH, DE, DK, ES, FI, FR, O	
(30) Priority Data: 60/005.974 08/584,040 11 January 1996 (11.01.96) (71) Applicants: RIBOZYME PHARMACEUTICAL: [US/US]; 2950 Wildemess Place, Boulder, CO 803 CHIRON CORPORATION [US/US]; 4560 Horto Emeryville, CA 94608 (US). (72) Inventors: PAVCO, Pamela; 705 Barberry Circle, L CO 80026 (US). McSWIGGEN, James; 4866 Drive, Boulder, co 80301 (US). STINCHCOMB, D Old Post Road, Boulder, CO 80301 (US). ESCO Jaime; 1470 Livorna Road, Alamo, CA 94507 (US) (74) Agents: HELLENKAMP, Amy, S. et al.; Lyon & Lyo Suite 4700, 633 West Fifth Street, Los Angeles, CA 2066 (US).	S, INGOI (US on Street Lafayett Frankl Dan; 720 OBEDO 5).	(88) Date of publication of the internation of the	he event of the receipt o

(57) Abstract

Nucleic acid molecule which modulates the synthesis, expression and/or stability of an mRNA encoding one or more receptors of vascular endothelial growth factor.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
AU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	1E	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE-	Kenya	RO	Romania
BY	Belarus	KG	Kyrgystan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic	SD	Sudan
CF	Central African Republic		of Korea	SE	Sweden
CG	Congo	KR	Republic of Korea	SG	Singapore
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	ŁK	Sri Lanka	SN	Senegal
CN	China	LR	Liberia	SZ	Swaziland
CS	Czechoslovakia	LT	Lithuania	TD	Chad
cz	Czech Republic	LU	Luxembourg	TG	Togo
DE	Germany	LV	Latvia	TJ	Tajikistan
DK	Denmark	MC	Monaco	TT	Trinidad and Tobago
EE	Estonia	MD	Republic of Moldova	UA	Ukraine
ES	Spain	MG	Madagascar	UG	Uganda
Fi	Finland	ML	Mali	US	United States of America
FR	France	MN	Mongolia	UZ	Uzbekistan
GA	Gabon	MR	Mauritania	VN	Viet Nam

Interno mail Application No PCT/ US 96/17480

A. CLASSIFICATION OF SUBJECT MATTER
1PC 6 C12N15/11 C12N9/00 C12N5/10 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 6 C12N C07K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Category ' Citation of document, with indication, where appropriate, of the relevant passages Relevant to claum No. Х WO 94 11499 A (MAX-PLANCK-GESELLSCHAFT ZUR 1-23 FÖRDERUNG DER WISSENSCHAFTEN E.V.) 26 May see page 30, line 18 - page 32, line 3 X WO 94 21791 A (J.E. BERGMANN AND 1,2,19 R.E.PREDDIE) 29 September 1994 see page 10, line 10 - line 26 Ε WO 97 00957 A (PRESIDENT AND FELLOWS OF 1-23 HARVARD COLLEGE) 9 January 1997 see page 34, line 12 - line 21 WO 95 04142 A (HYBRIDON, INC.) 9 February 1-23 1995 cited in the application see the whole document -/--Further documents are listed in the continuation of box C. Х Patent family members are listed in annex. Special categories of cited documents: "I" later document published after the international filing date or priority date and not in conflict with the application but 'A' document defining the general state of the art which is not cated to understand the principle or theory underlying the considered to be of particular relevance INVENTION 'E' earlier document but published on or after the international "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to 'L' document which may throw doubts on priority claim(s) or involve an inventive step when the document is taken alone which is cited to establish the publication date of another "Y" document of particular relevance; the claimed invention citation or other special reason (as specified) cannot be considered to involve an inventive step when the document is combined with one or more other such docudocument referring to an oral disclosure, use, exhibition or other means ments, such combination being obvious to a person skilled document published prior to the international filing date but in the art. later than the priority date claimed '&' document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 30.05.97 16 May 1997 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rapswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo ni. Cupido, M Fax (-31-70) 340-3016

national application No.

PCT/US 96/17480

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: 16-18 because they relate to subject matter not required to be searched by this Authority, namely: Remark: Although these claims are directed to a method of treatment of the human body, the search has been carried out and was based on the alleged effect of the claimed nucleic acid molecules.
Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
 claims 1-23 (all partly): Nucleic acid molecules specific for target sequences in the flt-1 gene. claims 1-23 (all partly): Nucleic acid molecules specific for target sequences in the flk-1/KDR gene insofar they are not included in invention 1 as defined in table X.
1. X As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest. X No protest accompanied the payment of additional search fees.

Internal Application No PCI/US 96/17480

		PC1/US 96	3/1/400	
	tion) DOCUMENTS CONSIDERED TO BE RELEVANT			
Category *	Citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.	
A	NUCLEIC ACIDS RESEARCH SYMPOSIUM SERIES, no. 31, 9 November 1994, page 163/164 XP002002020 USMAN N ET AL: "CHEMICAL MODIFICATION OF HAMMERHEAD RIBOZYMES: ACTIVITY AND NUCLEASE RESISTANCE"		1-23	
			<i>3.</i>	# to
				.:
•	·			
			•	ين الم

5

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

.ormation on patent family members

Internal Application No. PC1, US 96/17480

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9411499 A	26-05-94	AU 5562794 A CA 2149298 A CN 1094445 A EP 0669978 A JP 8505763 T	08-06-94 26-05-94 02-11-94 06-09-95 25-06-96
WO 9421791 A	29-09-94	NONE	
WO 9700957 A	09-01-97	AU 6288496 A	22-01-97
WO 9504142 A	09-02-95	AU 7516894 A CA 2167680 A CN 1131437 A EP 0711343 A FI 960374 A NO 960303 A	28-02-95 09-02-95 18-09-96 15-05-96 25-03-96 13-03-96

Form PCT/ISA/210 (patent family annex) (July 1992)